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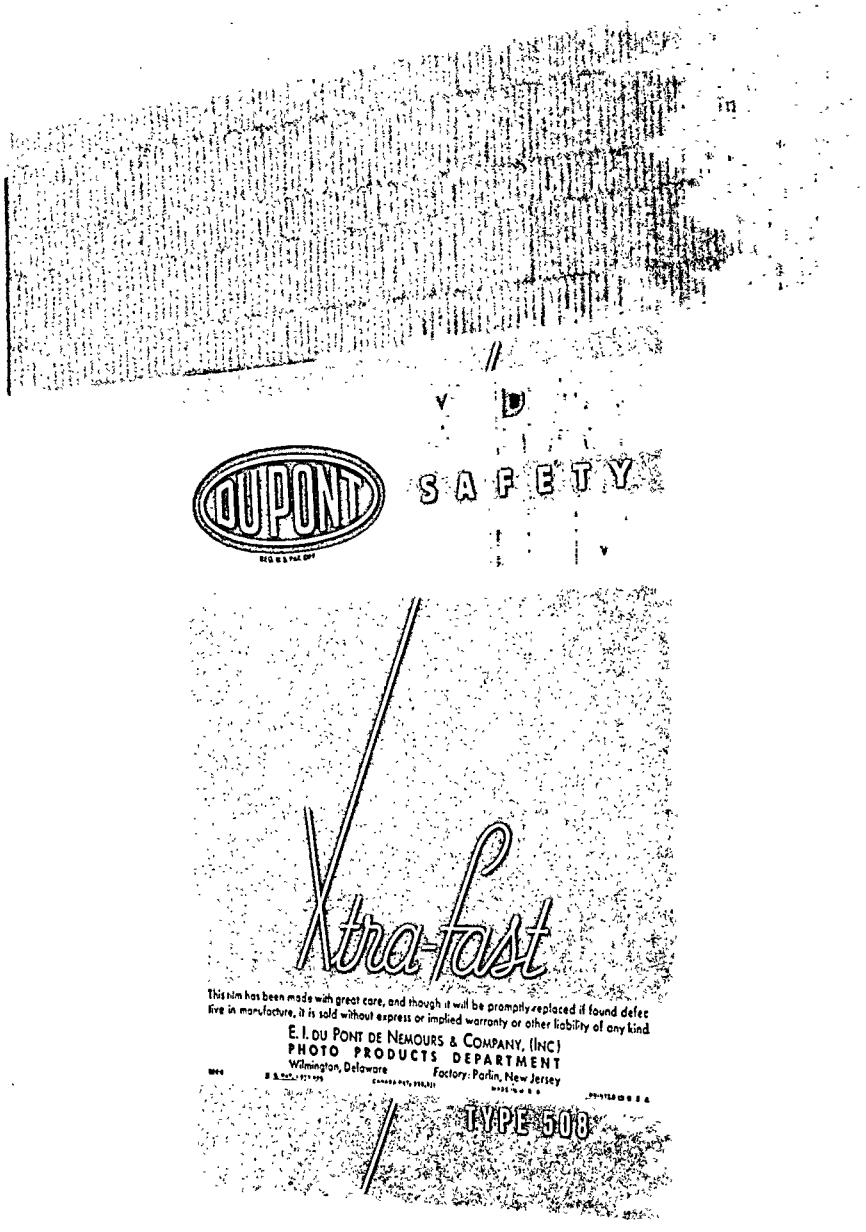
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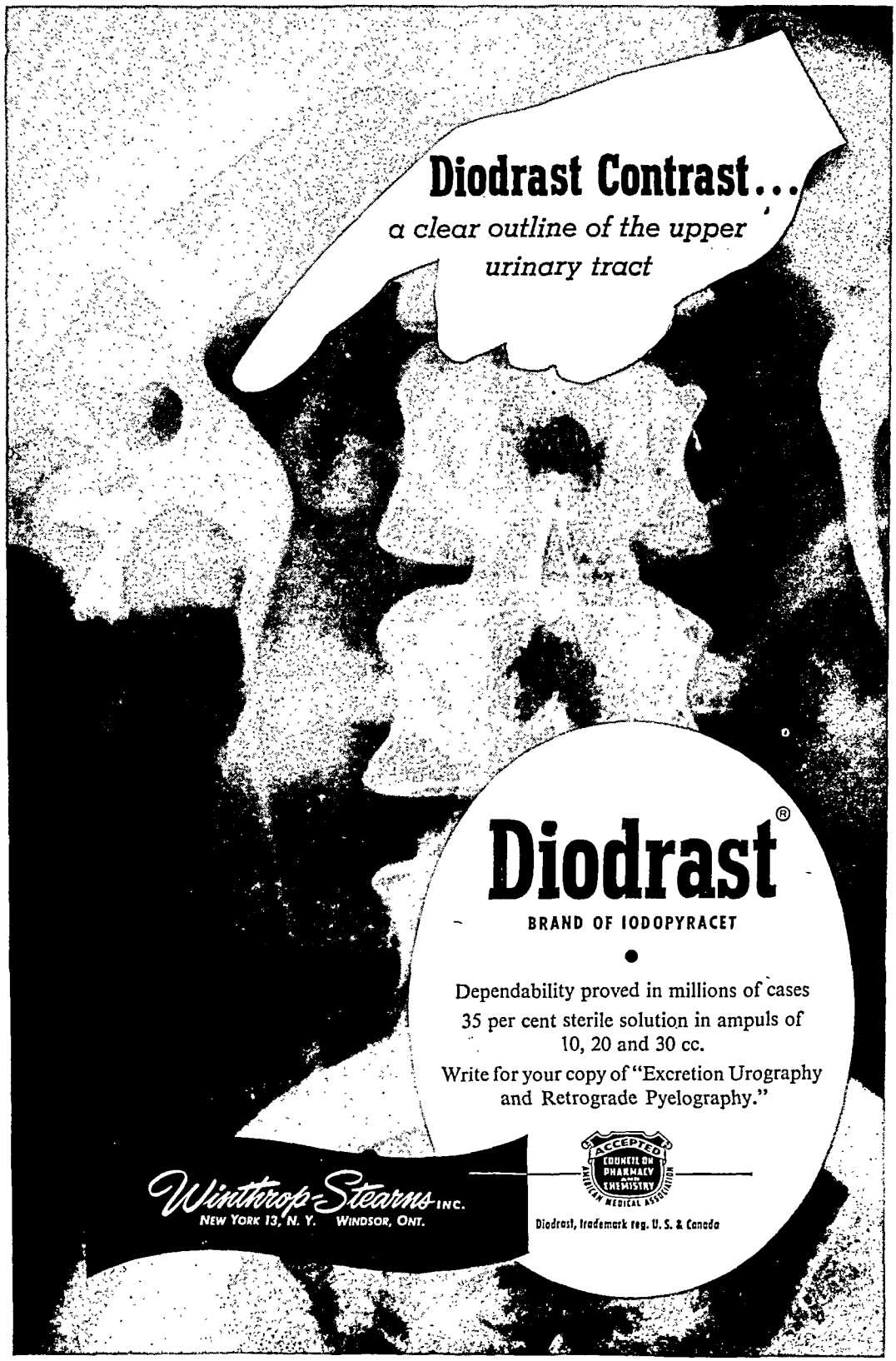
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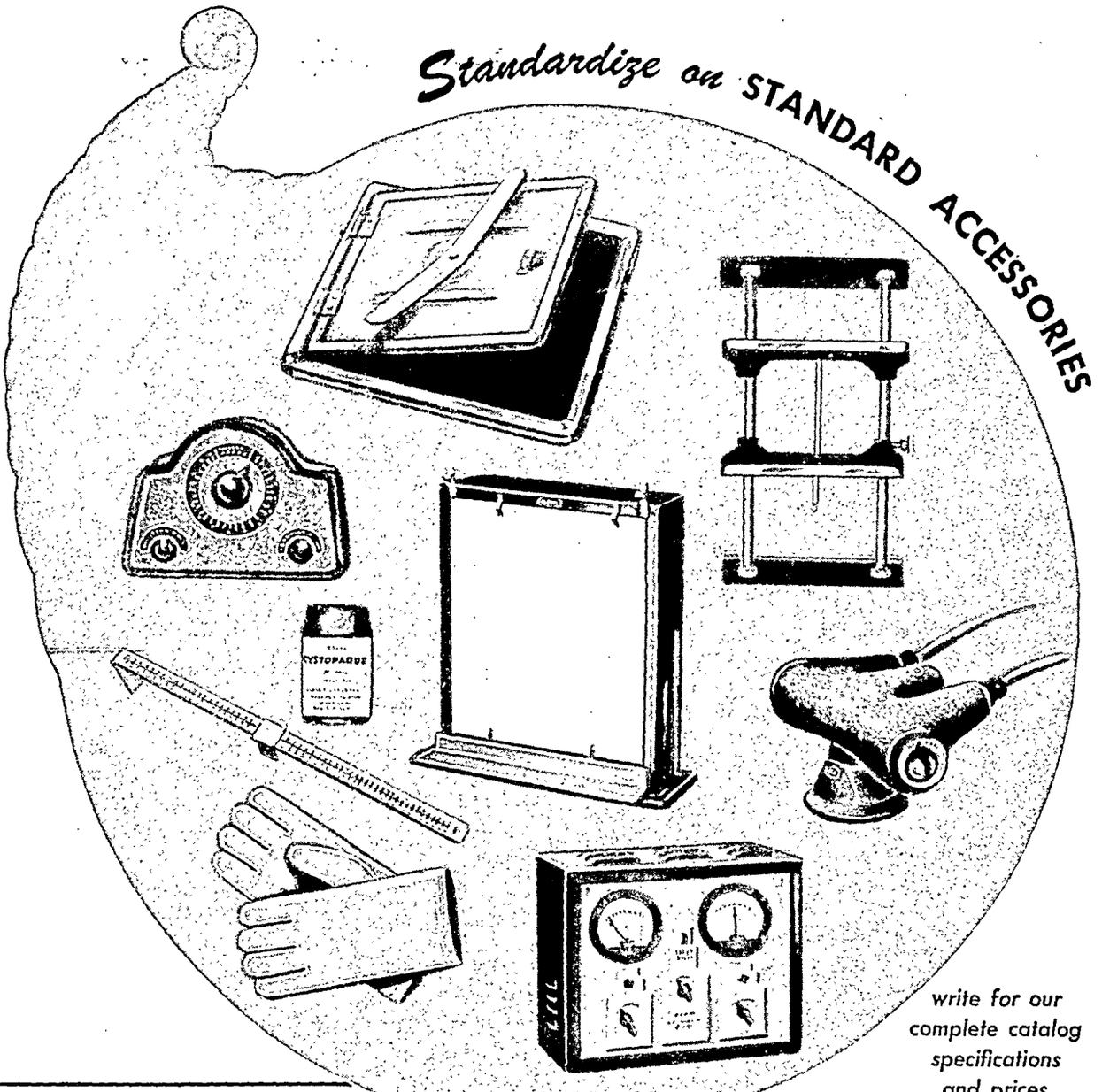
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CONTENTS

The Anatomy and Physiology of the Lesser Circulation as Indicated by its Behavior in Health and Disease L. R. SANTE, M.D. 1
Peripheral Vascular Disease in the Lungs ROBERT P. BARDEN, M.D., AND DAVID A. COOPER, M.D. 17
Lung Function ROBERT D. DRIPPS, M.D. 23
Conditions Which Result in Increased Pressure within the Lesser Circulation C. ALLEN GOOD, M.D., AND THOMAS J. DRY, M.D. 26
The Evaluation of the Lesser Circulation as Portrayed by the Roentgenogram W. WALTER WASSON, M.D. 30
The Value of Angiocardiography in Establishing the Diagnosis of Pericarditis with Effusion ROBERT G. WILLIAMS, M.D., AND ISRAEL STEINBERG, M.D. 41
A Rapid Method of Roentgenologic Examination of the Small Intestine. A Preliminary Report SYDNEY WEINTRAUB, M.D., AND ROBERT G. WILLIAMS, M.D. 45
The Procurement and Critical Appraisal of the Width Diameter of the Midline Retrogastric Soft Tissues . . M. H. POPPEL, M.D., F.A.C.R., ... A. SHEINMEL, M.D., AND E. MEDNICK, M.D. 56
Bone Sclerosis in Leukemia and in Non-leukemic Myelosis FRANK WINDHOLZ, M.D., AND SIDNEY E. FOSTER, M.D. 61
Lumbar Intervertebral Disc Protrusion Contralateral to the Side of Symptoms and Signs: Myelographic Verification in Two Cases J. P. MURPHY, M.D. 77
Bilateral Posttraumatic Ulnocuneiform Articulation HENRY MILCH, M.D. 80
Mixed Tumors of the Palate MAX CUTLER, M.D. 82
The Effect of Hyaluronidase on the Absorption of a Subcutaneously Deposited Radiopaque Substance NORMAN SIMON, M.D., AND LESTER NARINS, M.D. 91
Effect of Roentgen Rays upon Bartonella-*Infected and Normal Rats* DOROTHY NEUHOF NAIMAN, PH.D. 95
On the Association of Certain Hematomas with Myelencephalic Blebs in the House Mouse ARNOLD B. GROBMAN, PH.D. 98
Department of Technique
A New Processing Room Accessory: The "Clip Drip" Tray STANLEY H. MACHT, M.D. 100
Trifocal Glasses as an Aid to the Older Roentgenologist RAMSAY SPILLMAN, M.D. 102
Editorials
Nitrogen Mustard Therapy T. LEUCUTIA, M.D. 104
Eldwin R. Witwer, 1890–1948 . . . E. WALTER HALL, M.D. 108
José Francisco Merlo Gómez JAMES T. CASE, M.D. 110
Society Proceedings, Correspondence and News Items 111
Abstracts of Roentgen and Radium Literature 118

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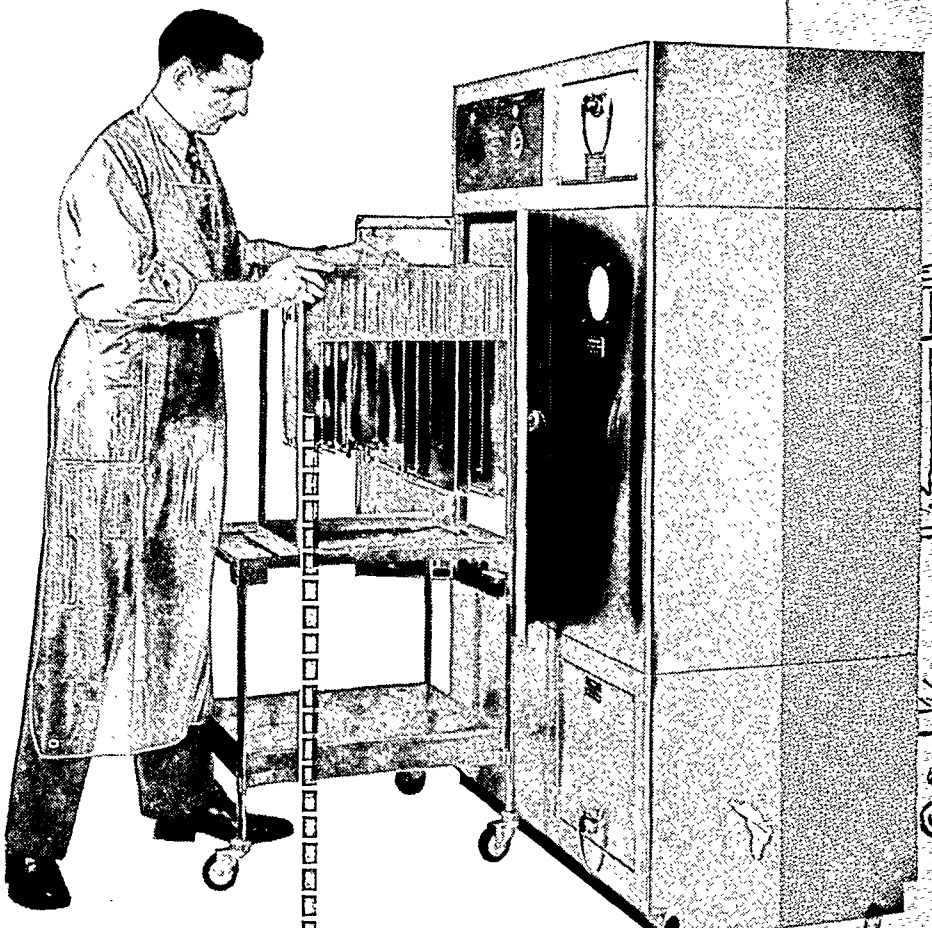
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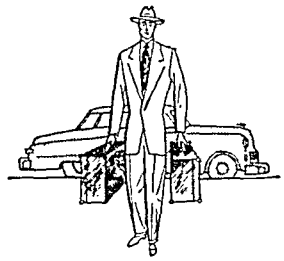
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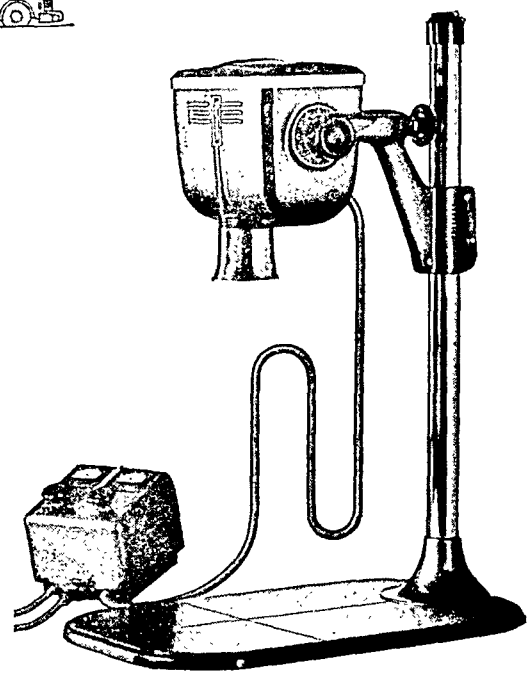
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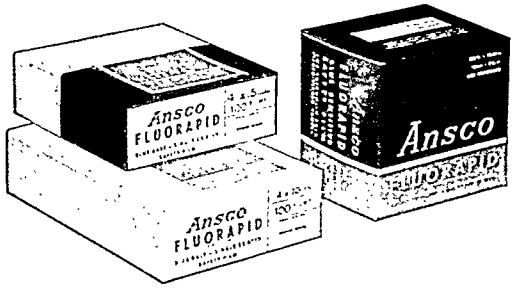
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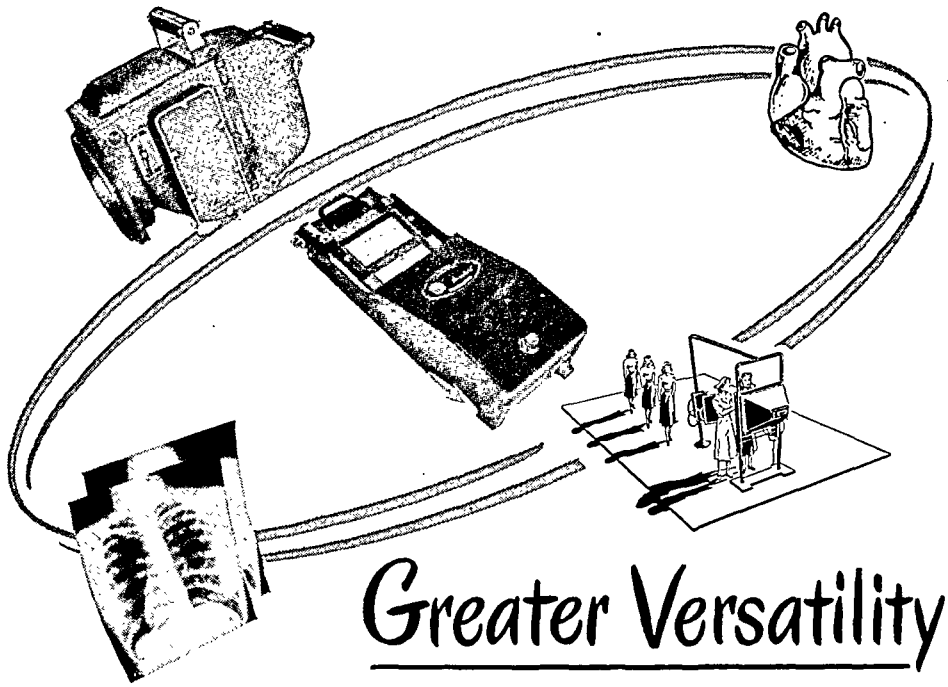
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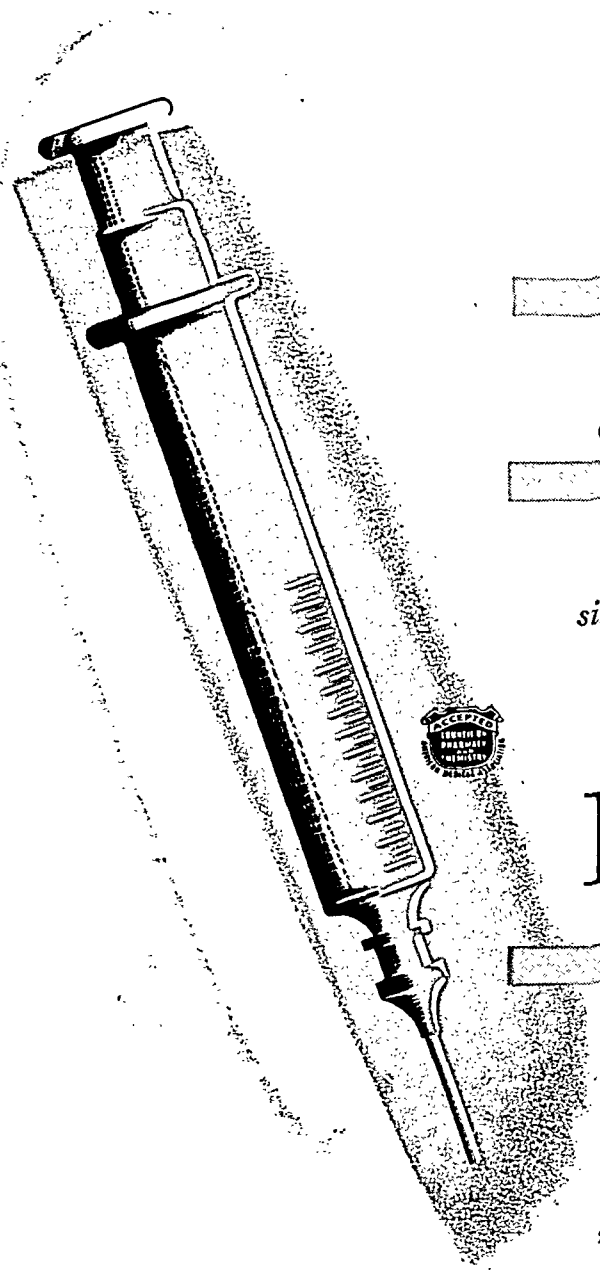
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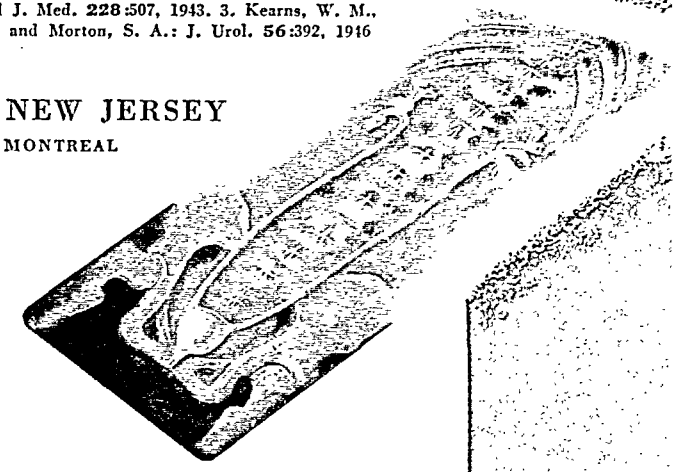
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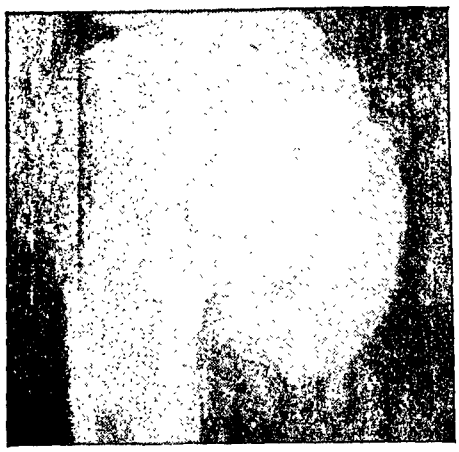
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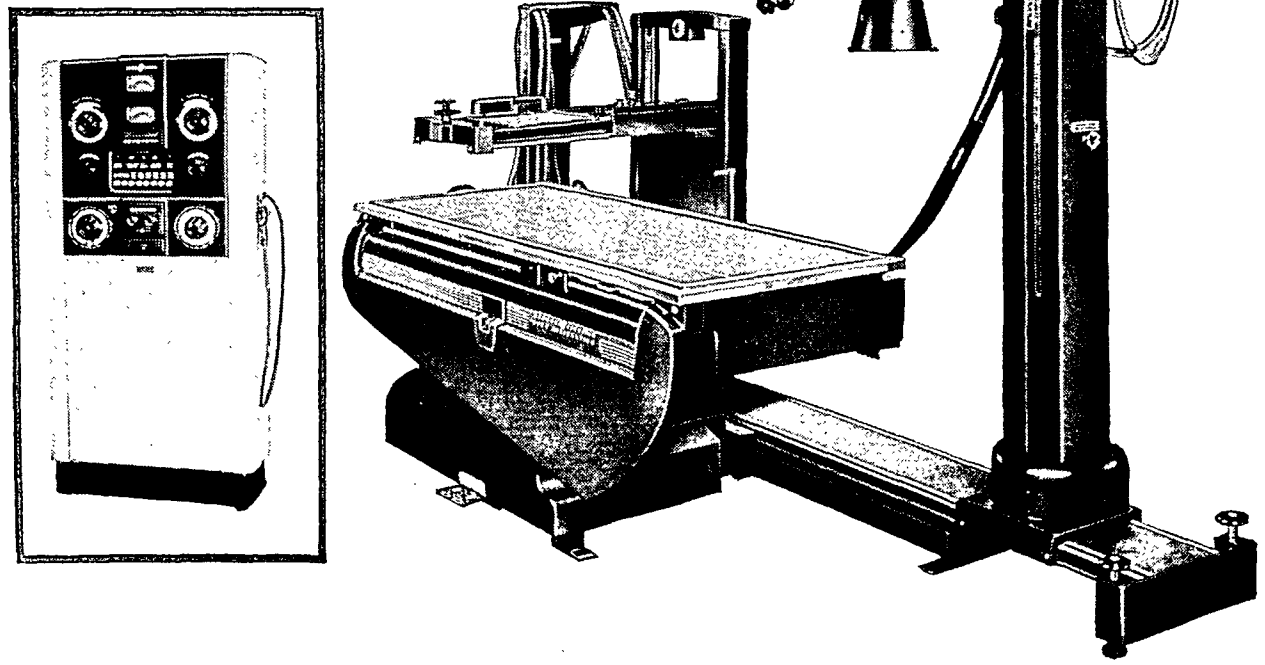
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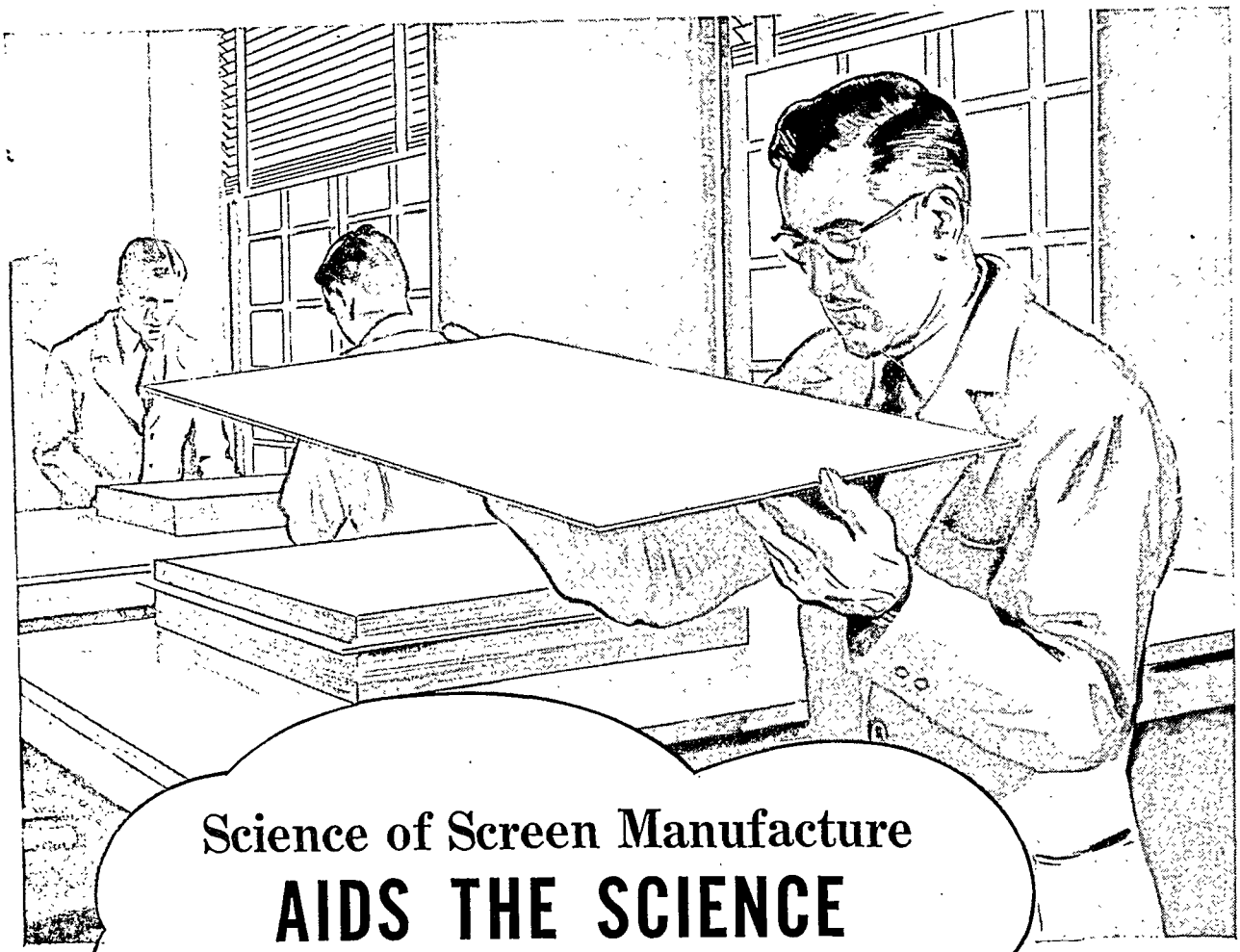
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VOL. 61 JANUARY, 1949 NO. 1

THE ANATOMY AND PHYSIOLOGY OF THE LESSER CIRCULATION

AS INDICATED BY ITS BEHAVIOR IN HEALTH AND DISEASE*

By L. R. SANTE, M.D.

ST. LOUIS, MISSOURI

ANATOMISTS and histologists have learned much about the minute structure of the lung by patient examination of innumerable microscopic sections. Physiologists, by ingenious experiments, have done much to clarify our understanding of its function. There still remains, however, many ambiguous phases of the entire subject of lung structure and function.

The roentgenologist, in his wide field of clinical observations, has a means of testing the validity of these findings in practice, and of making suggestions for their modification. All of the lung structures are interdependent; any condition affecting one will have some correlated effect upon the others. The purpose of this paper, therefore, will be to seek out the conditions in which the roentgenological and pathological findings may be of value in clarifying such fundamental points. The structures to be considered and their influence on the lesser circulation are:

Interstitial tissue—a structural framework for the lung composed of,
Fibrous stroma
Elastic fibers
Respiratory tract—having an intact epithelial lining from the trachea to the alveoli
Blood vessels—two sources, bronchial from the systemic circulation, and pulmonary, constituting the lesser circulation
Relation of capillaries to alveoli
Normal respiratory function
Increased alveolar pressure—emphysema
Decreased alveolar pressure—atelectasis
Vascular engorgement—passive congestion from cardiac failure
Vascular occlusion—infarction
Nervous and muscular control of bronchi—bronchiectasis
Lymphatics—anatomical relationship and function
Edema of lungs—absorption of protein and water.

INTERSTITIAL TISSUE

The view taken by Macklin[19,20] seems most plausible. He thinks of the interstitial tissue as being a construction framework for the lung, extending from the hilum to the finest air cells, offering passage from the bronchi, blood vessels and lymphatics, and giving strength through its fibrous stroma

* From the Department of Radiology of St. Louis University School of Medicine and St. Louis City Hospital. Presented at the Forty-eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16-19, 1947.



FIG. 1*a*. In a roentgenogram of the normal lung, the parenchymal structures show only in the peripheral zone. The terminal structures are so fine that the lung markings appear to feather out into imperceptibility.

for maintenance of the relationship of the other lung structures. The alveolar lining

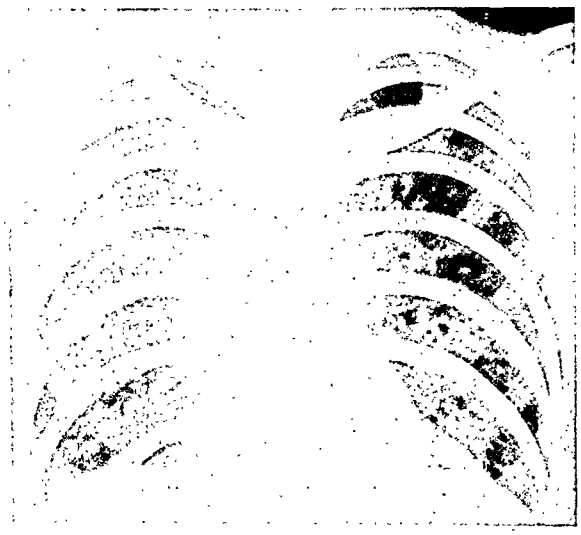


FIG. 1*c*. When the lung is involved by some disease which attacks the interstitial tissue, such as virus pneumonia, the existence of such interstitial tissue within the alveolar wall between epithelial layers of adjacent alveoli becomes quite evident. The infiltrative process seen in the peripheral zone of the roentgenogram is due largely to involvement of the interstitial tissue.

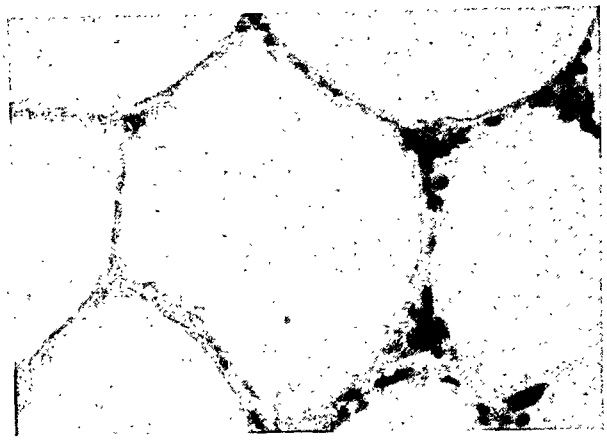


FIG. 1*b*. From the thinness of the mormal alveolar wall, it is hard to conceive the existence of interstitial tissue between the layers of alveolar epithelium of adjacent air cells.

is a continuous membrane of epithelial cells held in a close relationship to its surrounding capillaries and to each other by this fibrous tissue stroma in order to insure promptly coordinated reaction following changes in relationship of these structures. The stroma of the alveolar wall contains not only white fibrous tissue fibers but also yellow fibers of elastic tissue. "Stretching of the air sac walls is attended by a radial pull upon the vascular walls, and also by a longitudinal pull, just as with the walls of the air tract—bronchi, bronchioli and alveolar ducts. Deflation of the air space is accompanied by a recoil of the elastic tissue

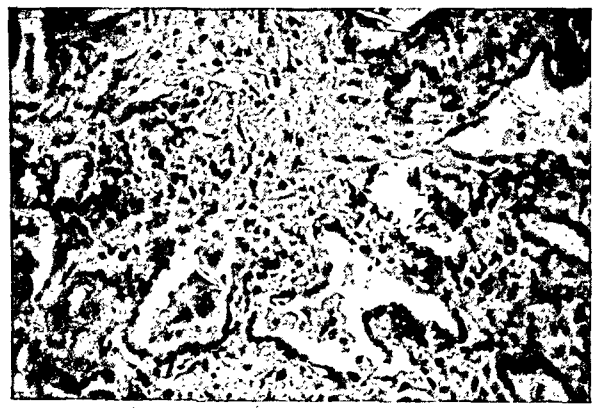


FIG. 1*d*. Contrast the enormous thickening of the alveolar wall in virus pneumonia due to interstitial involvement. Note two distinct layers of epithelium for adjacent alveoli with thick intervening interstitial tissue.



Fig. 2*a*. Anteroposterior and lateral roentgenograms of the chest. Air introduced into the mediastinum through a tracheotomy or other wound may be forced outward through the interstitial tissues of the lung to the finest lung structures, causing rupture of the alveoli, bilateral pneumothorax and death. This would indicate the existence of a continuous interstitial space throughout the lung.

and these spaces are all shortened and narrowed. . . . It is fortunate that the stroma is attached thus to the blood vessels, for otherwise there would not be this instant and favorable adjustment of their walls and calibre to the needs of the inspiratory phase."

It is true that the septum between adjacent alveoli (Fig. 1*a*, *b*), on microscopic examination seems hardly wide enough to represent two layers of epithelial cells, one for each alveolus, with intervening interstitial tissue for passage of blood vessels. Microscopic examination of sections of the lung, however, from patients infected with certain diseases, such as virus pneumonitis (Fig. 1*c*, *d*) which attack the interstitial tissue, shows marked thickening of the interstitial space with cellular infiltration, and inflammatory reaction of the intact alveolar cell membranes (Sante).[30]

In the hilar regions the interstitial tissue is large in amount offering passage for the bronchi, blood and lymph vessels; the bronchi are supported by cartilaginous rings, but the vascular structures are not so firmly constructed. The fibrous interstitial tissue about the vessels arranges itself into tough perivascular sheaths. That these perivascular sheaths are continuous, extending throughout the interstitial space from the hilum to the terminal air cells in one direction and back into the mediastinal space in the other, is indicated by the pathway traveled by air which gets into the interstitial tissue of the lung (Fig. 2*a*, *b*) (Macklin[18,21]). Interstitial emphysema may originate in the periphery from rupture of an emphysematous bleb (Sante[28]), extend-



Fig. 2*b*. Microscopic examination shows air in the interstitial spaces surrounding the vascular structures, as it spreads to the periphery to the finest lung structures.

ing to the mediastinum and producing the appearance of a halo about the heart characteristic of air in the mediastinal space. Or the air may gain entrance into the mediastinum directly through an operative incision from tracheotomy or other wound. Large amounts of air sucked into the mediastinal space in this manner spread rapidly through the interstitial framework of the lung to the periphery causing rupture of the lung and pneumothorax. Microscopic examination shows the air in the perivascular spaces of the interstitial tissue. Pressure from this entrapped air upon the vascular wall interferes with circulation of the blood and may cause death. This is perhaps the most convincing proof of a continuous interstitial space from the periphery of the lung, back through the root of the lung and into the mediastinum.

RESPIRATORY TRACT

The gross anatomy of the lung is quite clearly understood (Brock[5]); the finer lung structures, comprising the minute anatomy of the lung, still require clarification on some points.

William Snow Miller's[23] microscopic study of the primary lobule of the lung is a classical foundation for further consideration and investigation. His observations will be recalled that, as the bronchi extend toward the periphery, they continue to divide and subdivide until they reach a point where the cartilaginous rings, which form a supporting framework for the bronchioles, disappear, leaving only the musculature and fibrous stroma for the support of the bronchioles. At this point in the bronchial subdivision the bronchioles have air cells opening off directly from their walls which prompts their designation as respiratory bronchioles. From this location the bronchioles divide and subdivide into ductulus alveolaris, atria, sacculi alveolares, terminating finally in alveoli pulmonum or terminal air cells.

The portion of the lung structure distal to the respiratory bronchiole may be considered as the parenchymal tissue of the lung. Roentgenological examination after the intratracheal injection of iodized oil will serve to trace these divisions of the bronchial tree to the minutest structures. This would indicate that there is an intact epithelial lining of some sort for the respiratory structures from the bronchi to the terminal air cells.

Some observers maintain that no separate alveolar epithelium exists and that the capillary walls of the blood vessels form the lining membrane of the alveoli contained in a ground substance directly exposed to the alveolar air, with occasional "septal cells" probably of mesenchymal origin (Lang,[15] Bloom,[4] Loosli[17]). Certain microscopic sections showing cuboidal cells extending part way around the alveolar membrane apparently gives support to this contention (Aschoff,[1] Seemann,[31] Bargmann[2]) but these are probably due to bronchioles cut obliquely. Others feel that the alveoli are formed by an intact epithelial lining and that the capillaries form an independent syncytial network covering them (Miller,[23] Bremer[3]). It is difficult to understand how the capillary walls could themselves form the lining of the alveoli and still present an intact circulation. This would imply a transition of bronchial to vascular epithelium at some point beyond the respiratory bronchiole. This seems hardly possible since Miller[23] has traced the bronchial epithelium peripherally to the terminal alveolar structure. Furthermore, he has demonstrated in microscopic section an intact ring of epithelial cells lining the alveolus. It is true that this was in an edematous lung which, in the strictest sense of the word, could not be considered as an absolutely normal structure, but such an argument seems illogical since no pathological lesion exerts less injury to cells, nor excites less reaction than transitory edema; it is, in fact, merely a physiological response to variations in fluid pressures within the lung. There is hardly any other condition which can develop more rapidly and subside more quickly with complete restoration of the lung to normal. In the case of

mechanical edema of the lungs (Moragues[21]), which developed immediately after rupture of one of the papillary muscles of the heart causing death within a few hours, time would hardly permit the proliferation of cells to form a complete alveolar lining. This is convincing although not absolute proof of the existence of a separate epithelial layer of alveolar cells. If the vascular epithelium formed the alveolar lining of adjacent alveoli on either side, it would imply the non-existence of interstitial tissue between the alveolar walls.

VASCULAR STRUCTURE OF THE LUNG

The respiratory bronchiole is an important landmark also in the pulmonary circulation. The blood supply of the lung is from two sources, the pulmonary and bronchial vessels. The pulmonary arteries, carrying venous blood to the lung for aeration, accompany the bronchi, dividing and subdividing as they extend toward the periphery, sending minute branches to the finest subdivisions. These minute vascular branches have been used by Miller,[23] in tracing the finest respiratory subdivisions to their termination. A corresponding system of pulmonary veins returns the aerated blood to the heart. *The bronchial arteries*,[23] carrying arterial blood, act as *nutrient vessels to the bronchi* and are imbedded in their walls up to the region of the respiratory bronchioles; at this point the bronchial and pulmonary circulations mix in a plexus of capillaries which cover the lung beyond this region; *nourishment of the parenchymal* tissue of the lung, therefore, comes largely from the *pulmonary vessels*.

RELATION OF CAPILLARIES TO ALVEOLAR STRUCTURE

The structure and arrangement of the capillaries in relation to the alveoli are of greatest importance. It is obvious that they must form a thin vascular network covering the alveoli and that they must be shielded, in some way, during deep inspiration from pressure of the distended alveoli, between which they lie. We know that during inspiration the volume of the chest cavity is much increased in size due to the action of the musculature of the thoracic walls and diaphragm (Best and Taylor[3]). This increase in volume is taken up both by an increase in air and blood content. It has been shown that the blood volume in the lung increases as much as 50 per cent during deep inspiration. This is a means of producing greatest aeration of the blood. In order for this to take place and for the thin-walled capillaries to withstand pressure from the distended alveoli there must be some structural safeguard. This is found in the elastic tissue which runs in strands within the fibrous stroma, like guy wires over the alveolar membrane.[23] The exact location of the elastic fibers is difficult to show microscopically but their function should serve to indicate their location. Their purpose is to limit and prevent overdistention of the alveolar structure and to offer recoil elasticity to the alveolar wall. Like elastic fibers in any location they offer more and more resistance as they undergo greater and greater distention. They are imbedded in the stroma and extend over the alveolar epithelium forming a part of the alveolar wall. The capillary network covers the alveoli intervening between adjacent alveolar structures. The fibrous stroma covering the capillaries holds them in intimate relationship to the alveolar walls but does not contain elastic tissue elements. The elastic fibers could not extend over the capillary network since if this were true alveolar distention would produce vascular constriction and thus prevent maximum aeration during inspiration.

Normally, the small venules in the lung which supply the capillary network are also closely surrounded by the alveoli; in fact, the alveoli which abut on the walls of the venules serve to aid in the support of the vascular wall—the amount of intervening interstitial tissue is very small. It is obvious then that any change in size of the surrounding alveolar structure or any change in the interalveolar pressure will be transmitted directly through the thin-walled

vessel, thus helping to equalize any changes which may take place between the alveoli and the circulation.

Macklin's observation,[19] "because the expansile force of the incoming air is spread by means of the perivascular sleeve of air cells, over the arterial and venous systems rather than being concentrated upon the pulmonary capillaries . . . it is felt that the capillaries are protected from possible harm," seems quite valid. That the "expansile force of incoming air" is not an independent force acting upon the capillary walls, however, but rather a passive response to the negative pulmonary pressure producing it, which acts *alike* on both *capillaries and alveolar walls*, must not be overlooked. The gradient of force acting upon the air cells, and capillaries concerned in carrying on the function of the lung, has been fully discussed by Wasson.[32]

The alveolar walls are guarded from overexpansion by elastic fibers whereas the capillaries have only a fine fibrous stroma. The increase in blood volume in the lung during deep inspiration is explained by the fact that the *blood capillaries* thus guarded from pressure by overdistention of the *alveoli are themselves subject to changes in intrathoracic pressure* so that the development of a negative pressure in the thorax during inspiration produces greater vascularity as well as greater engorgement of the blood capillaries in contact with the alveolar membrane, all desirable effects in aeration of the blood. The pull of the stroma maintains the close relationship of the capillaries to the alveolar walls and aids in their expansion and elongation. On *expiration*, pressure of the distended alveoli on the capillaries squeezes out the excess blood, thus producing a pump-like action which is a very potent factor in aiding the pulmonary circulation.

Roentgenographically, the increased illumination of the lung field during deep inspiration indicates the relatively greater percentage of air-to-blood content in the lung. Westermark[33] has shown roentgenographically the effect of pressure on the capillaries of the lungs while in their fully inflated state, by the Valsalva exercise (forced expiration against obstruction). Under such circumstances the air pressure in the distended alveoli is increased by attempting forced expiration against the closed mouth and nose; the marked blanching of the lung field as shown on roentgen examination during this procedure is indication that the capillaries are subject to further action in expressing still more blood from the vascular structures by thoracic pressure.

This would indicate the close relation of the blood capillaries to the alveolar structure of the lung; their prompt response to changes in alveolar function; the protection of the alveoli by elastic fibers within the alveolar walls, and of the blood capillaries by the spread of the forces exerted by alveolar changes to all of the vascular structures.

Increased Alveolar Pressure—Emphysema. Let us consider the effect of increasing alveolar pressure as in pulmonary emphysema (Fig. 3*a* and 3*b*). One may judge the function of the elastic tissue on the lung structure by considering the effect produced in pathological conditions in which it is congenitally absent or destroyed. Emphysema is probably produced by defects in the elastic tissue structures either inherent or acquired. In this condition the restraint which is normally present on alveolar distention is removed, the alveolar pressure rises and the alveoli become enormously enlarged and overdistended even to the point of rupture. Likewise, the elastic recoil of the lung is impaired so that the air content is never properly expelled. As a result, the distended alveoli squeeze the capillary network, preventing proper circulation of the blood, with resulting dyspnea and cyanosis.

Roentgenographically, this is indicated by increased radiolucency of the lung, but little if any change in illumination during inspiration or expiration. The Valsalva exercise likewise does not show any change in the illumination of the lung fields, indicat-

ing that there is very little displacement of blood from the already impoverished pulmonary circulation. The pressure of the distended alveoli likewise is exerted upon the smaller bronchioles interfering with all but the slightest passage of air to the alveolar structure. As a result, it is seen that iodized oil injected into the bronchial tubes will not pass out into the alveolar structure, but remains confined to the larger bronchial branches (O'Donoghue[26]).

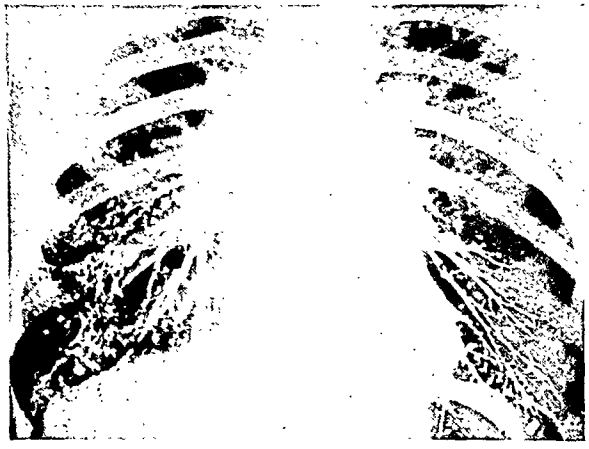


Fig. 3*a*. The best way to demonstrate the function of the elastic tissue fibers in the alveolar wall is to study the behavior of the lung where these fibers are deficient. In emphysema the intra-alveolar pressure becomes increased due to failure of elastic tissue to express the air on expiration; the unrestrained distention of the alveoli during inspiration squeezes the unprotected intervening capillaries and as a result there is not only enormous dilatation and rupture of the alveolar walls but marked avascularity of the lungs as well. Lipiodol injected into the emphysematous lung does not proceed down into the alveolar structure due to the increased intra-alveolar air pressure.

Emphysematous bullae, formed by overexpansion of the alveolar structures from the check-valve action produced by pressure on their ducts may even be outlined by the oil-filled bronchioles; the oil does not enter the bullae. Within twenty-four hours the oil will be expelled from the emphysematous lung. Normally, iodized oil injected in this way will pass out into the alveolar structures producing a feathery appearance on roentgen examination which will remain for many months. *In obstructive emphysema*, however, the overdistended alveoli have their elastic fibers intact, merely squeezing blood out of the lung by their dilatation as shown roentgenographically by hyperaeration of the lung and return to normal after relief of obstruction. In this respect compensatory emphysema differs from emphysema of the hypertrophic type.

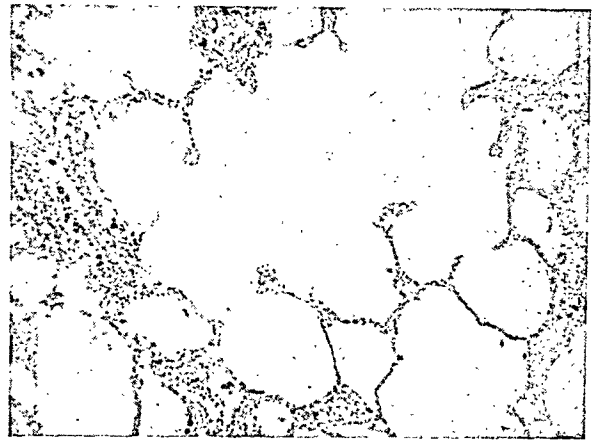


Fig. 3*b*. Microscopic examination in pulmonary emphysema reveals distention, or breakage through, of the alveoli from increased intra-alveolar pressure. Unrestrained pressure within the alveoli causes almost complete avascularity of intervening capillaries.

Decreased Alevolar Pressure—Atelectasis. In normal inspiration the lung expands passively by an inrush of air, as a result of enlargement of the chest cavity; the negative force is exerted from *outside* the alveolus and the inrush of air occurs to equalize the pressure. If a bronchus is completely occluded by a plug of mucus, foreign body, or from other cause, the peripheral lung segment will become atelectatic and collapse from absorption of the entrapped air. In atelectasis, then, the process is reversed; the suction force produced by absorption of alveolar air is exerted from *within* the alveolus (Fig. 3*c* and 3*d*). Diffusion of gases through the alveolar membrane continually takes place in order to equalize the atomic pressure. The capillary circulation continually offers a fresh supply of blood for aeration whereas the alveolar air is blocked in

the alveolus and cannot be renewed. The suction force thus created within the alveoli is tremendous. Elastic tissue prevents overdistention of the air cells in maximum inspiration but there is nothing to restrain them from complete collapse. Just how does the pulmonary circulation fare under such conditions? We have seen that the capillary network is almost directly exposed to all changes in intrathoracic pressure; only the slight resistance from the capillary wall is interposed. The pumping action of respiration is suspended; the sucking action of air cells produced by continuous absorption of the alveolar air is exerted directly upon the vascular walls also; both are factors in producing engorgement of the circulation. In this instance the force is so great that the chest wall is drawn down, the diaphragm displaced upward and the mediastinal structures pulled over to the affected side. Such force directly applied to the walls of the vascular organs of the lungs should be very potent in producing an engorgement of the lung vessels, especially of the capillary structures. The extreme density of the lung field (as dense as lobar pneumonia) is evidence of vascular engorgement. The prompt disappearance of the lung consolidation with reinflation of the lung, after rolling the patient upon the unaffected side, is added indication that vascular engorgement is responsible for the increased lung density (Sante[27]).

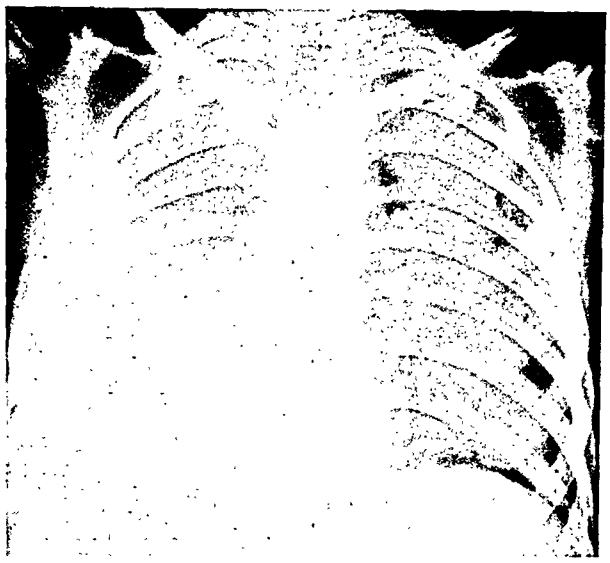


FIG. 3*c*. Decreased intra-alveolar pressure occurring in atelectasis results in a sucking action exerted on the alveolar walls. The alveoli are protected by elastic tissue from overdistention but there is no action in protecting against excessive deflation. As a result, there is engorgement of the capillaries and other blood vessels of the lungs. It is this vascular engorgement which imparts to the atelectatic lung the extreme roentgenographic density. The engorgement occurs in passive response to the sucking action of decreased intra-alveolar pressure and therefore there is little if any edema of the lung.

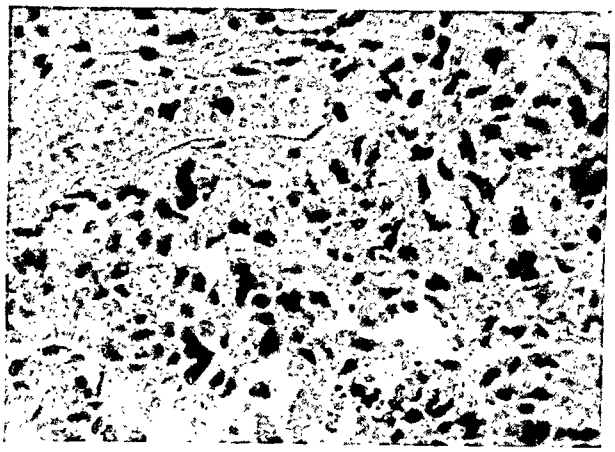


FIG. 3*d*. Microscopic section of pulmonary atelectasis. Note collapse of alveolar walls, widening of interspaces between alveoli, and marked capillary engorgement.

Roentgenological as well as clinical evidence would indicate that there are two forms of massive atelectatic collapse of the lung, the one due to bronchial occlusion by a single gelatinous inspissated plug of mucus, the other resulting from profuse secretion which may have its origin as an exudate from the parenchymal structures, the so-called "drowned lung;" both causing atelectasis because of bronchial occlusion from loss of the cough reflex. In the dry type, re-expansion takes place immediately, within a few minutes, following rolling the patient on the uninvolved side and the expectoration of a single "glob" of mucus which "stands up like a gumdrop on the bottom of the cup;" in the "drowned lung" type re-expansion takes place more slowly; the patient coughs up greater quantities of thinner sputum before re-expansion takes place.

If a single lobe is involved, the sucking action produced by the atelectatic process is transmitted to the adjacent aerated lung causing compensatory emphysema. It is interesting to note, by lipiodol injection, that the suction force is not equally divided throughout the lung but is most pronounced in the immediate vicinity of the collapsed lobe.

We know that the healthy alveolar membrane will also permit air to pass directly through from one to another adjacent lobule, since air injected into one bronchiole can readily be demonstrated coming out of an adjacent bronchiole of the same lobe. Small openings or pores between adjacent alveoli have been demonstrated microscopically (Miller[23]). This mechanism helps to equalize the pressure in adjacent air cells. One would think, therefore, that segmental collapse (atelectasis) of small portions of the lung would be impossible since air deficiency would be replaced from adjoining alveoli. But we know that segmental collapse does occur, so that our only conclusion must be that with the development of the slightest edema or infiltration this permeability of the alveolar membrane is lost. This is as it should be since the greater the distention of an alveolus and the greater the pressure of its air content, the more pervious it should become. We know of course that the greatest degree of aeration of the blood takes place when the alveoli are distended with air during inspiration and that, conversely, the more collapsed the alveoli, the more reduced the alveolar pressure; this should favor greater obstruction to the passage of air between the alveolar walls. Partial obstruction of a segment of the lung may result in segmental emphysema (Golden[12]).

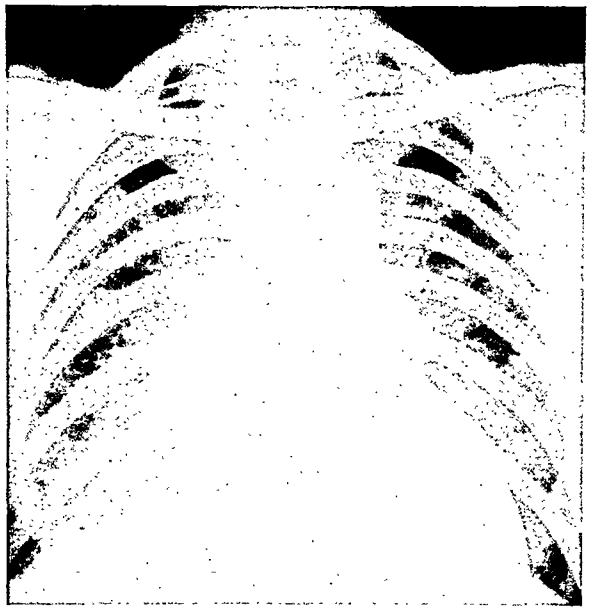


Fig. 4*a*. Passive pulmonary congestion produces in the roentgenogram a more or less characteristic picture: engorged vascular trunks radiate fan-shaped outward from both hilar regions into the periphery of the lung. The outer parenchymal zone is clear, however.

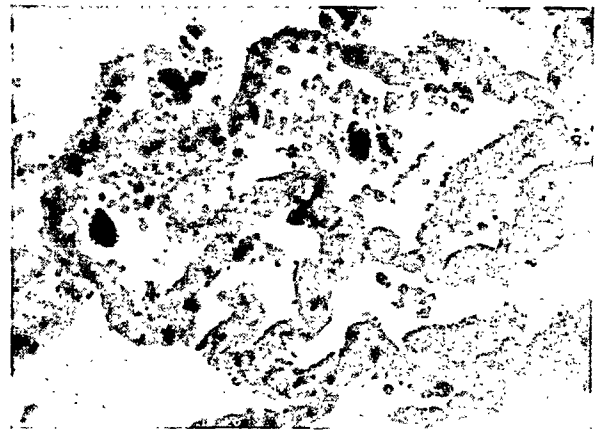


Fig. 4*b*. Microscopic findings in passive pulmonary congestion shows the enormously distended capillaries between the alveolar walls without evidence of intra-alveolar edema.

Vascular Engorgement. Passive congestion of the lung produces engorgement of the capillaries due to failure of cardiac action (Fig. 4, *a*, *b*, *c*, *d*). Stasis results and the capillary network becomes packed with red blood cells but they remain within their capillary walls as long as compensation is maintained.

Roentgenographically the stage of passive pulmonary congestion results in an increase in blood vascular markings radiating outward from the hilar region into the lung.

Pulmonary Infarction. Blood clots orig-

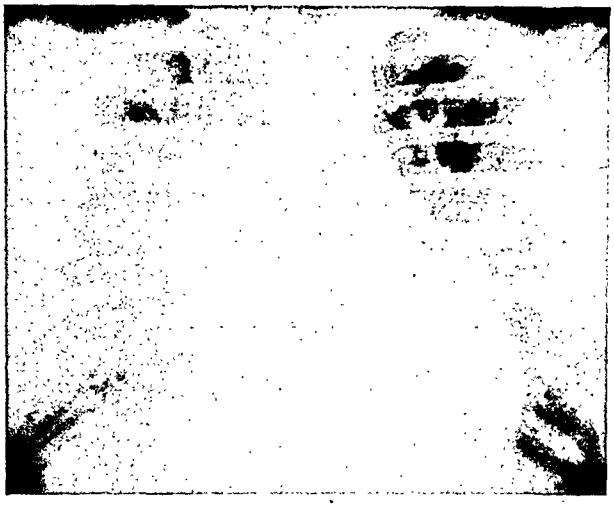


FIG. 4*c*. Edema of the lungs results when the pressure within the blood vessels exceeds the interalveolar pressure and serum exudes from the blood vessels into the alveoli.

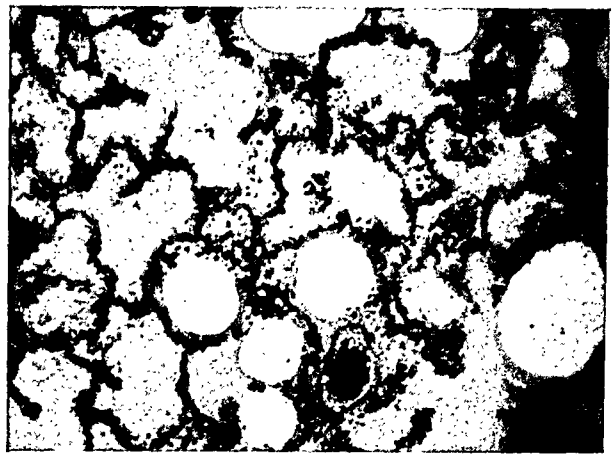


FIG. 4*d*. Microscopically edema of the lungs shows the fluid within the alveolar spaces. This cuts off the blood from aeration, producing an ever-increasing degree of anoxemia.

inating in the systemic circulation or heart may lodge in the pulmonary circulation forming emboli (Fig. 5*a* and 5*b*). Such emboli are not visualized in the roentgenogram since they are of the same density as the blood stream. Westermark has shown, by utilizing the Valsalva exercise, that blanching of the obstructed region occurs. If collateral circulation is adequate for nutrition of the structures, true infarction may not take place and the tissues may be restored to normal. Blood supplied by anastomosis with the adjacent capillaries and by the bronchial artery may be sufficient to prevent the death of the tissues. The bronchial artery is peculiarly adapted to this purpose; it arises from the systemic circulation (the aorta) so that it is not likely that anything should happen to it at the



FIG. 5a_1. Infarcts of the pulmonary circulation have a tendency to occur at the periphery of the lung where the planes of the pleura form an angle with each other. These become consolidated, showing in the roentgenogram as areas of increased density, margins perpendicular to the pleural plane, inner edge may be rounded and smooth.

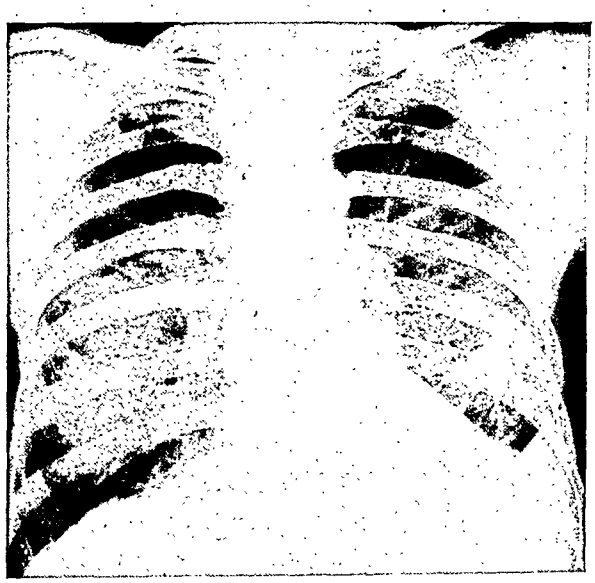


FIG. 5a_2. Organization of infarcts commences almost immediately. Even within a few days microscopic evidence of beginning organization is present; complete organization requires several weeks.

same time that infarction of the pulmonary circulation occurs. If the blood supplied from these sources is not sufficient to maintain the nutrition of the lung structure in the involved area, infarction occurs.

Then, and then only, does the infarct become visible in the roentgenogram. It has been found that infarcts usually occur at the periphery of the lung when two planes of the pleura meet the infarcted area showing a medial rounded border.[13] Just why infarcts occur in such regions is not definitely known but it probably is due to some particular arrangement of the vascular structures in these locations.

When an embolus lodges in the pulmonary vessel, the blood supply to the parenchymal structure from that source is cut off, and the area that it supplies is dependent upon blood borne by the bronchial artery and the collateral capillary circulation. Stasis occurs and blood exudes from the capillaries into the lung structure, producing a hemorrhagic infarct. Organization by scar tissue formation begins almost at once and is evident microscopically within a few days.

Unless the infarct becomes infected it rarely undergoes necrosis.

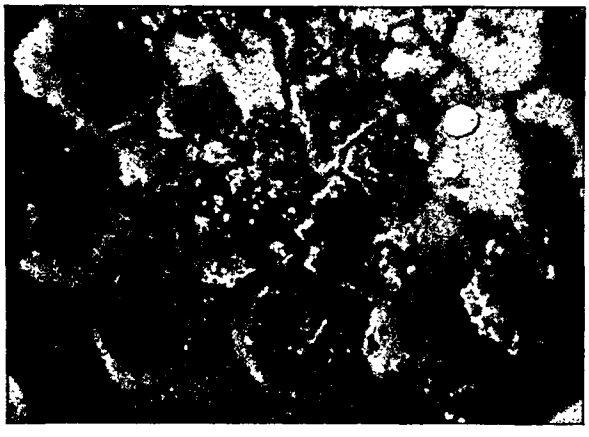


Fig. 5*b*. Hemorrhagic infarct of the lung. The lung is one of the few organs of the body provided with two circulations, the pulmonary and the bronchial. When the pulmonary circulation is blocked the bronchial artery pours blood into the area from the systemic circulation providing nutrition for the infarcted area.

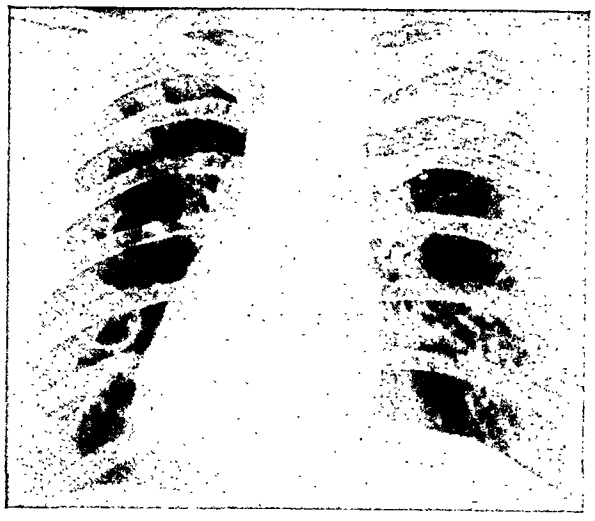


Fig. 5*c*. Infarcts involving the bronchial artery as well as the pulmonary vessels, caused by infection having a predilection for blood vessels, cause thrombosis, result in formation of nodules at the periphery of the lung which rapidly undergo central liquefaction producing thick-walled annular shadows of unusual type.

Thrombosis, on the other hand, resulting from infection by an organism having a predilection for vascular structures, may result in complete occlusion of the bronchial circulation as well (Fig. 5*c* and 5*d*) (Sante and Hufford[29]). Under such circumstances necrosis rapidly follows, even in a matter of hours. Rounded nodules varying from 0.5 to 3 cm. in diameter appear

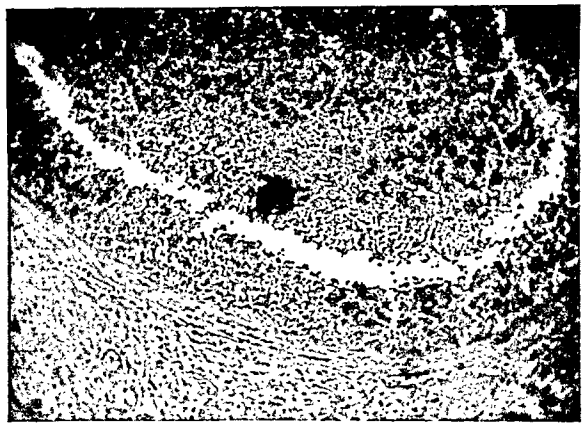


Fig. 5*d*. Thrombosis of bronchial as well as pulmonary vessels from infection. This results in rapid formation of unusual annular shadows throughout the lung.

throughout the lung fields; these rapidly liquefy in the center leaving smooth annular shadows having thick but uniform walls.

These probably represent the line of demarcation between viable and destroyed tissue of the infarcted lobule. They may become thinner and thinner and ultimately disappear, or may remain evident in the roentgenogram for more than a year later.



FIG. 6*a*. In bronchiectasis the bronchial dilatation is limited to the distribution of a bronchus usually involving an entire lobe. In the roentgenogram the dilated bronchial branches extend peripherally to a point which would correspond to the respiratory bronchiole; the zone of normal appearing lung beyond is probably due to compensatory emphysema of the adjacent normal lung.

Microscopic sections show thrombosis in all of the vessels with evidence of an infection in the surrounding tissue.

Nerve and Muscular Control of Bronchi—Bronchiectasis. Bronchiectasis is primarily a disease of the smaller bronchi (Fig. 6). A consideration of the vast amount of experimental investigation, pathological and clinical observation (Lisa and Rosenblatt[16]) which has been carried out on the subject would indicate that bronchiectasis is caused primarily by severe infection of the bronchial wall. The mucosa is stripped up and the bronchial wall thus denuded is subjected to extension of the infection to the other bronchial structures: the muscle wall, elastic tissue, nerve fibers, and the blood vessels. Irregular areas of necrosis occur in these tissues, severing their continuity and thereby rendering them functionally useless. These have always seemed to me to be the essential factors in development of bronchiectasis. During normal respiration, the bronchi become larger in caliber and longer during inspiration, and smaller and shorter during expiration. This is due to the influence of neuromuscular control; muscle tone maintains the normal configuration of the bronchus due to the action of the same structures. In bronchography it has been noted that cocainization of the bronchus produces marked dilatation, and removes the natural diameter changes ordinarily observed in normal bronchi during respiration. These are exactly the same conditions which prevail in bronchiectasis, the bronchial wall loses its tone, dilates and no longer responds to respiratory changes. Add to this infection which has invaded and destroyed areas in the bronchial wall and

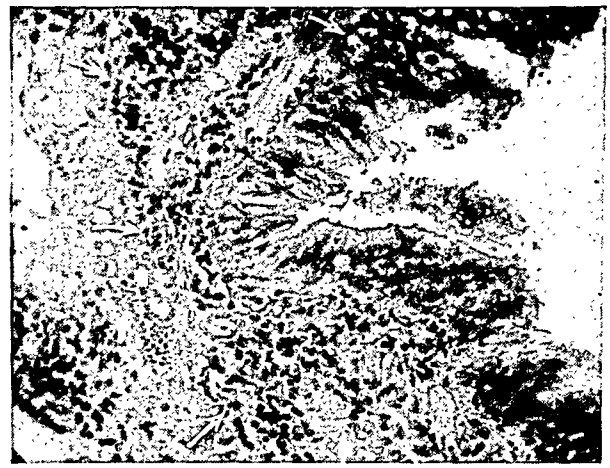


FIG. 6*b*. Microscopic examination in bronchiectasis shows destruction of bronchial mucosa, with undermining and stripping up of epithelium by infection; and destruction of the bronchial musculature, thus removing its support from the bronchial wall and permitting dilatation of the bronchus.

the picture is practically complete. There still remains the alveolar structure to be accounted for; edema alone, resulting from such profound infection, would be sufficient to cut off the parenchymal structure supplied by the involved bronchus. Atelectasis of such a small volume of lung tissue followed by fibrosis would hardly be detectable in the roentgenogram. As this small volume of atelectatic or scar tissue contracts, the space is filled in from either side by compensatory emphysema from the adjacent alveoli. As the acute infection subsides the areas of destruction in the bronchial wall heal with fibrous tissue formation and the non-flunctioning state of the bronchial musclature becomes permanent. Epithelization of the chronically infected bronchus completes the picture.

Roentgenographically, lipiodol readily enters and outlines these blind bronchial pouches and shows they have no muscular tone. The failure of any alveolar filling to occur from these bronchi, and the ease with which they are emptied, indicates that their parenchymal lung tissue is destroyed. The distance observed between the end of the blind pouch and the pleural surface indicates the size of bronchus involved by the process.

The Lymphatic Structures of the Lung. Again the region of the respiratory bronchiole is an important spot. From this point the lymphatic drainage of the lung progresses in two directions, one toward the hilum by the lymphatic trunks which accompany the vascular system, the other toward the periphery of the lung to the pleura, over its surface terminating likewise in the hilar region. Valves in the lymphatic vessels prevent reverse flow. The smallest lymphatic divisions do not extend to the alveolar structure but end at the alveolar ducts. The function of the lymphatics is to absorb any proteinized fluid which may escape from the vascular structures and return it to the blood stream, thus guarding against its loss to the body; likewise, to absorb any form of foreign material such as coal dust or bacteria, filtering them out by their glandular structures, as pointed out by Drinker[10]. The lack of lymphatic structures peripheral to the alveolar ducts would indicate that the alveolar membrane would have to become extremely swollen and edematous and fluid would have to exude into the alveoli before it would be subject to absorption by the lymphatics. Such fluid may be disposed of either by coughing and expectoration, in which case it is lost to the body, or by absorption of the protein either in its unchanged state or after being broken down by enzymes, in which case it is restored to the body. Krogh[14] has pointed out that anoxia increases the permeability of the capillaries. There is a loss of blood volume with concentration of corpuscles in the capillaries and a reduced volume flow which further reduces the delivery of oxygen to the tissues and thus a vicious circle is established. Krogh further states that the capillary status resulting from oxygen deficiency is irreversible after fifteen minutes. As Drinker[9] appropriately points out, "anoxia begets anoxia."

A case reported by Moragues[24] of spontaneous rupture of a papillary muscle of the heart affords a good example of purely mechanical acute engorgement of the lung. The patient was stricken while eating his lunch and survived only a few hours. Autopsy revealed extreme vascular engorgement and extreme edema of both lungs.

It is evident that pulmonary edema, if it occurs in any sizable area of the lung may become very dangerous; this is especially significant in surgical cases and should be guarded against by all possible means (Chase[7]).

As Drinker[10] points out, one would expect to find large lymphatic vessels draining into the thoracic duct so that there would be the freest possible movement of the lymph toward the great veins but that no such arrangement usually exists; instead, all lymph from *both lungs*, except for a small area in the left apex, drains by way of the right lymphatic duct into the right subclavian vein. This right lymphatic duct

"is an exceedingly short and small vessel, and is thus a definite bottleneck at the end of a widespread system of lymphatic vessels."

If the pulmonary vein is obstructed, there is an immediate increase in the lymph flow from the right thoracic duct, indicating that there is an immediate transudation through the capillaries into the tissues and then into the lymphatics. Passive pulmonary congestion associated with cardiac decompensation results in similar retardation of blood flow and produces similar results. The lymphatics protect the body from loss of protein substance; any inadvertently lost in the tissues is absorbed by the lymphatics and returned to the circulation by the subclavian vein.

The fluid and electrolyte balance between the tissues and the vascular and lymphatic structures is maintained by the hydrostatic osmotic pressure on either side of the permeable membrane. Drinker[10] points out that " . . . in any consideration of a balance of forces the membrane itself must never be forgotten; and when the membrane is living, it may vary in permeability almost as rapidly as hydrostatic pressure change, and infinitely more rapidly than alterations occur in concentration of blood protein, upon which the colloid osmotic pressure depends. It is my belief—that simple pulmonary edema and the more serious pulmonary exudations depend more upon alterations in the permeability of the lung capillaries than upon complicated pressure relations in the pulmonary circulation." Just how great an influence the nervous system has in regulating the permeability of these walls is not known but extensive research would indicate that there is a definite regulatory mechanism (Bülbring and Whitteridge[6]). The colloid osmotic pressure is about 25 to 30 mm. of mercury throughout the systemic as well as the pulmonary circulation, but the capillary blood pressure in the lungs is about one-half to one-third that present in capillaries of the body tissues elsewhere. Whereas the body tissue should be just on the verge of spilling fluids into the tissues, the lung tissues should show greater assurance of a dry lung.

This would also explain the pronounced absorptive powers of the normal lung. Water aspirated in to the lung is rapidly absorbed *by the capillaries* provided there is an intact circulation; it does not result in increase in lymphatic flow (Courtice and Phipps[8]).

Water is an essential substance for the continued normal function of the body. The chemical composition of fluids contained in various structures of the body differs greatly. Muether[25] states, "It is obvious that the plasma and interstitial fluids are practically identical except for the amount of protein which is much higher in plasma than in interstitial fluid. This indicates that the extracellular electrolytes can be easily pass to and from the intravascular and interstitial fluid. . . . Exchange between the blood and the interstitial fluid is accomplished primarily by variations in the capillary blood pressure and protein content of the interstitial fluid, on the one hand, and the tissue tension and serum proteins, on the other."

The mechanism of thirst usually serves to maintain the fluid balance under normal conditions; under certain abnormal circumstances, however, it may be necessary to utilize other parenteral methods for administration; subcutaneous, intravenous, intracavitary, or into the marrow cavities of bones (Muether[25]). All of these are subject to the regulatory mechanism of absorption except the intravenous method which not only dumps the increased load of fluid upon the circulation but serves to dilute the blood and disturb the fluid balance.

While the danger of overhydration is looked upon lightly by the surgeon, the roentgenologist sees many cases in which too rapid administration of large amounts of fluid results in spilling over of fluid into the interstitial and alveolar structures of the lung. The shifting of such edematous areas to the most dependent portion of the lungs by change in position of the patient is indication that dependency is a factor in

its production. Many factors enter into the development of such a "spill over" from the circulation which are fully appreciated and can be avoided (Elman,[11] Marriott[22]).

To recapitulate: The lymphatics do not surround the alveolar structures like the blood capillaries; the right lymphatic duct drains the lungs but is inadequate in most instances to take care of excess quantities of exudate rapidly forming, thus producing a bottle-neck in the flow of lymph from the lung. This would indicate that the regulation of fluid balance in the lung structures is a complicated mechanism depending upon the water-electrolyte balance between the capillaries and surrounding tissues and the state of the intervening permeable membrane. The lymphatics have to do with the absorption of protein which is spilled over into the tissues and its return to the blood stream. Excess water, on the other hand, is readily absorbed by the capillaries.

SUMMARY

The principal function of the lung is the aeration of the blood; the two structures concerned in this function, the blood-containing capillaries and the air-filled alveoli, come into relationship in the terminal air cells. All of the anatomical arrangements here described are concerned with the fulfillment of this function.

Gaseous interchange takes place between the alveolar air and the blood by diffusion of gases through the alveolar lining and capillary wall. This is the process which takes place with each normal respiration. Anything which interferes with this normal mechanism will have an influence on the respiratory function.

The behavior of the respiratory function under various pathological conditions involving the lung structures has been described and discussed. A knowledge of the microscopic pathology should aid in the understanding of the roentgen manifestations produced by these diseases.*

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* For discussion see page 37.

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PERIPHERAL VASCULAR DISEASE IN THE LUNGS*

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AN ATTEMPT has been made in previous papers[1,2] to outline the pathologic conditions which produce changes in the peripheral blood vessels of the lung and to illustrate the roentgen appearance of the chest in some of them. The radiologist should recognize that vascular disease may produce characteristic shadow patterns which differ from those which accompany disease of the lymphatic or alveolar pulmonary structures.[3] Furthermore, conditions which produce obstruction or obliteration of peripheral vessels may be distinguished from those accompanied by increased permeability of the vessel walls. However, a clear understanding of the pathology and clinical features of the group of diseases in question (Table 1) is essential, and serial roentgen examinations are often necessary before an accurate differential diagnosis can be made.

TABLE I

SOME CONDITIONS WHICH MAY PRODUCE CHANGES IN THE SHADOWS OF THE PERIPHERAL VASCULAR SYSTEM IN ROENTGENOGRAMS OF THE CHEST

1. Vascular Congestion	
	Heart failure, congenital heart disease, hemangioma
2. Intrinsic Obstruction of Blood Vessels	
	Thrombosis and embolism, trauma, polycythemia, leukemia, parasites, tumor emboli
3. Intrinsic Disease of Blood Vessel Walls	
	Sepsis, syphilis, arteriolar sclerosis, rheumatic fever, scleroderma
4. Obliteration of Vessels by Adjacent Pulmonary Disease	
	Pneumonia, tuberculosis, silicosis, carcinoma, abscess, emphysema
5. Hypersensitivity States and Toxins Causing Increased Permeability	
	Periarteritis nodosa, exfoliative dermatitis, influenza, lupus erythematosus, glomerulonephritis, eclampsia, beriberi, sulfa poisoning.

ILLUSTRATIVE CASES

1. *Congestive Lesions.*

Pulmonary hemangioma.

CASE 1. A. L., female, white, aged fifty, complained of cyanosis and chronic cough with occasional hemoptysis for many years. Examination showed multiple subcutaneous hemangiomas, most prominent over the dorsum of each hand. Hemoglobin 110 per cent, red blood cell count 7,000,000, white blood cell count and differential normal. Bone marrow smear showed nothing abnormal. Serial roentgenograms of the chest revealed unchanging nodular shadows scattered through both lower lung fields which were thought to represent pulmonary hemangiomas (Fig. 1).

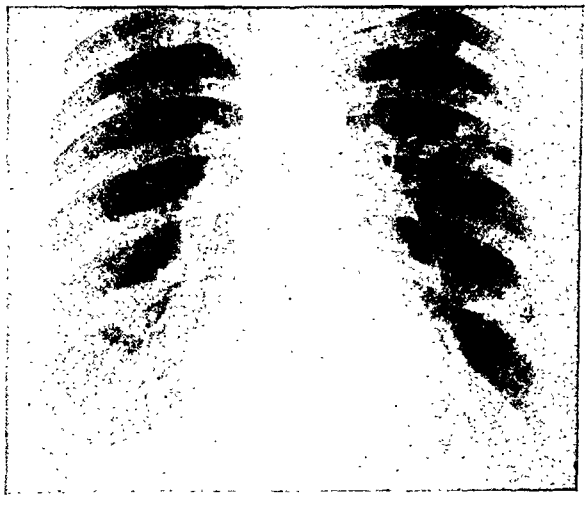


FIG. 1. Case 1. Roentgenogram of the chest of a patient with dyspnea, cyanosis and polycythemia (probably secondary type). The multiple nodular shadows in the lower lung fields were thought to represent hemangiomas because of the associated extensive cutaneous hemangiomas which the patient presented. Note the irregular shape of the nodules and the lack of a sharp border.

* From the Department of Radiology and the Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia. Presented at the Forty-eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16–19, 1947.

Comment. Although final confirmation is lacking in this case, the association of the pulmonary shadows with the polycythemia and subcutaneous hemangiomas make a diagnosis of pulmonary hemangiomas tenable. Additional proof might have been obtained by careful roentgenoscopy which should show pulsation of the nodules and diminution in their size when the patient performs forced expiration against the closed glottis.[9,10]

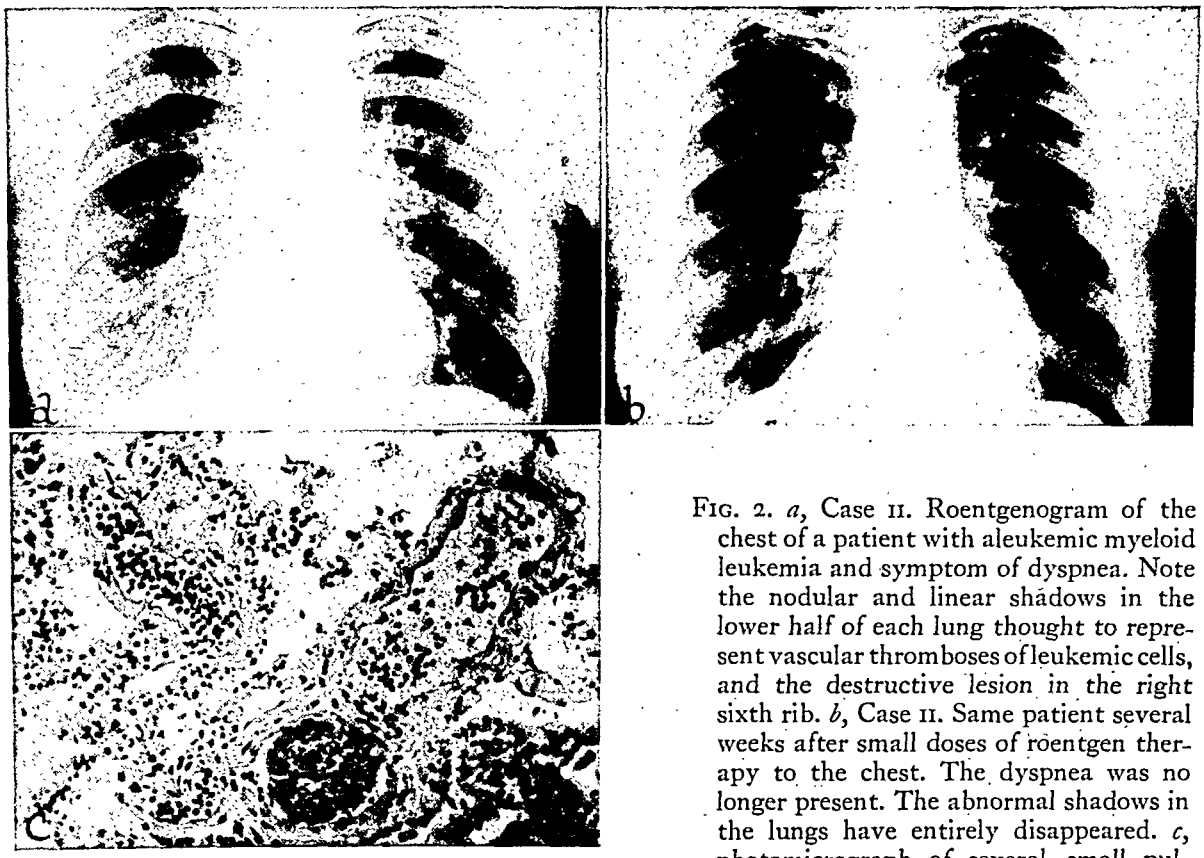


FIG. 2. *a*, Case II. Roentgenogram of the chest of a patient with aleukemic myeloid leukemia and symptom of dyspnea. Note the nodular and linear shadows in the lower half of each lung thought to represent vascular thromboses of leukemic cells, and the destructive lesion in the right sixth rib. *b*, Case II. Same patient several weeks after small doses of roentgen therapy to the chest. The dyspnea was no longer present. The abnormal shadows in the lungs have entirely disappeared. *c*, photomicrograph of several small pulmonary blood vessels from a patient with a similar history. In the lower center is a vessel with an organized thrombus containing degenerating leukemic cells. At one and eleven o'clock are vessels cut sagittally, containing excessive numbers of leukemic cells and probably undergoing early thrombus formation.

2. *Intrinsic Obstruction of Pulmonary Vessels.*

Leukemia.

CASE II. M. T., female, white, aged fifty-two, complained of enlarged lymph nodes, subcutaneous nodules, anema, and purpura of two years' duration. Intermittent cough and dyspnea were relieved by roentgen therapy. The peripheral white blood cells were normal, but the bone marrow smear showed myeloid leukemia. Roentgenogram of the chest about a year after the onset of her illness showed many nodular shadows in the lower half of each lung field and a pleural reaction at the bases (Fig. 2*a*). Several weeks after roentgen therapy to the chest, these shadows all disappeared (Fig. 2*b*). The lesions were thought to be due to leukemic thromboses of pulmonary vessels or possibly interstitial infiltrations. (See Fig. 2*c*, photomicrograph from a patient with a similar history.)

Comment. Thromboses due to leukemic cells occur so frequently in this disease that their appearance in pulmonary vessels is to be expected. The roentgenologist should include such a possibility in his interpretation when nodular shadows are seen in the lungs.

Carcinoma.

CASE III. V. F., male, white, aged thirty-nine,

archeologist known to have had several tropical diseases. Complained of chronic cough, increasing dyspnea, weakness and anemia for four years. All studies were negative except for sputum repeatedly positive for *Monilia*. Serial roentgenograms showed diffuse linear and nodular shadows in the lung, becoming progressively confluent until they resembled a "snow storm" just before death (Fig. 3, *a* and *b*). Because of the duration of the illness, the process was considered an infection, possibly moniliasis. Postmortem examination showed carcinoma of the bile ducts with emboli in the pulmonary vessels (Fig. 3*c*). The tumor was peculiar in that it produced marked connective tissue reaction which "choked" it by dense scarring and accounted for its protracted course.

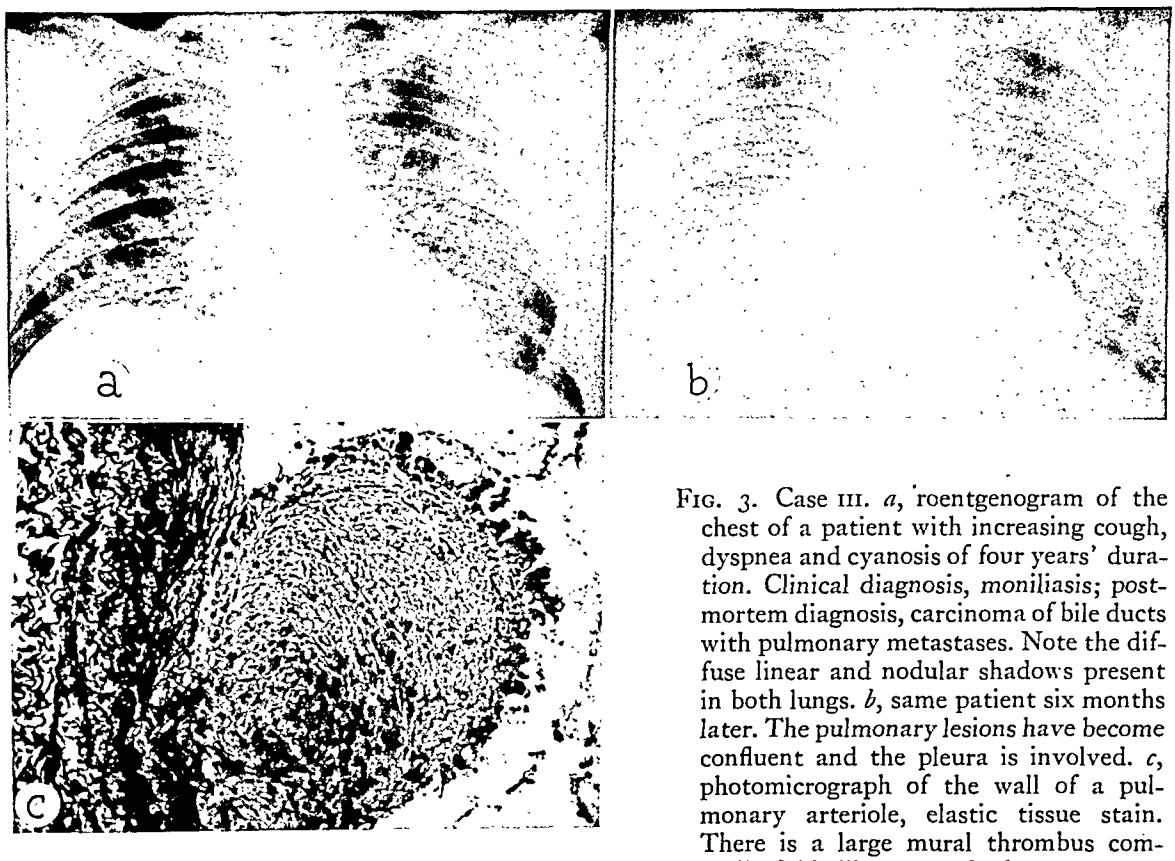


Fig. 3. Case III. *a*, roentgenogram of the chest of a patient with increasing cough, dyspnea and cyanosis of four years' duration. Clinical diagnosis, moniliasis; postmortem diagnosis, carcinoma of bile ducts with pulmonary metastases. Note the diffuse linear and nodular shadows present in both lungs. *b*, same patient six months later. The pulmonary lesions have become confluent and the pleura is involved. *c*, photomicrograph of the wall of a pulmonary arteriole, elastic tissue stain. There is a large mural thrombus composed of connective tissue with a rim of degenerating tumor cells. This illustrates the hematogenous spread of the tumor, and the restraining effect of the connective tissue reaction to it which accounted for the protracted course of the disease.

Comment. This sequence of events is not rare with tumors of the biliary and gastrointestinal tracts. Occasionally, a patient may present right heart failure, because of the extent of the pulmonary vascular occlusion by metastases, as the first symptom of such a tumor.[6]

3. *Intrinsic Disease of Vessel Walls.*

Acute rheumatic fever.

Case IV. E. S., male, white, aged twenty-five, with known rheumatic heart disease. Acute exacerbation with sore throat, fever, rash, and abdominal pain. Living and well ten years later. Roentgenogram at height of the illness showed a diffuse hazy shadow obscuring the upper half of each lung without evidence of cardiac failure (Fig. 4*a*). After recovery, follow-up roentgenograms have revealed an unchanging pattern of diffuse, symmetrical nodulation, probably representing organization of areas of perivascular exudation, possibly with deposition of hemosiderin (Fig. 4, *b* and *c*).

Comment. This is a good example of the

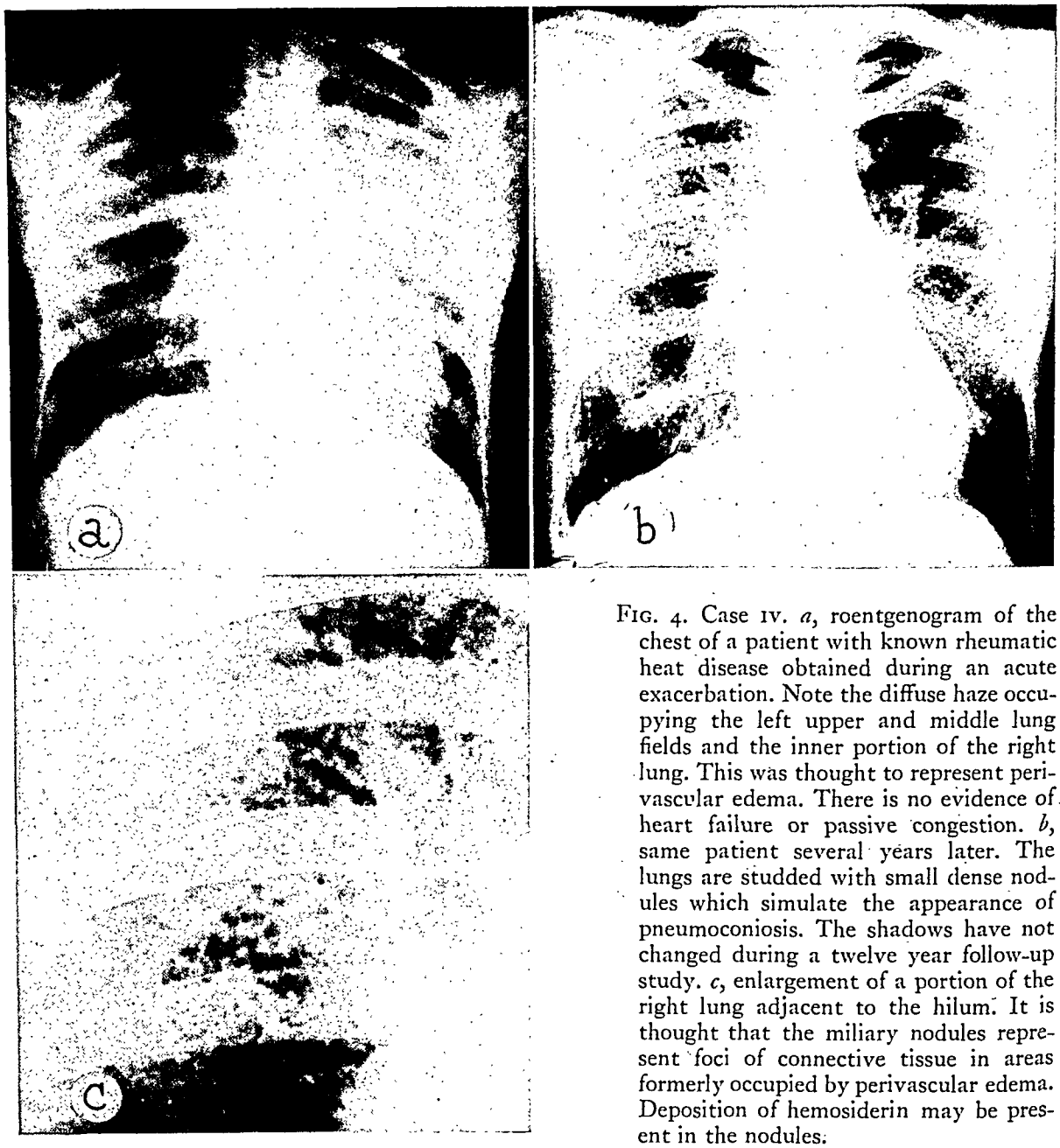


FIG. 4. Case IV. *a*, roentgenogram of the chest of a patient with known rheumatic heat disease obtained during an acute exacerbation. Note the diffuse haze occupying the left upper and middle lung fields and the inner portion of the right lung. This was thought to represent perivascular edema. There is no evidence of heart failure or passive congestion. *b*, same patient several years later. The lungs are studded with small dense nodules which simulate the appearance of pneumoconiosis. The shadows have not changed during a twelve year follow-up study. *c*, enlargement of a portion of the right lung adjacent to the hilum. It is thought that the miliary nodules represent foci of connective tissue in areas formerly occupied by perivascular edema. Deposition of hemosiderin may be present in the nodules.

controversial "rheumatic pneumonia." The acute lesion of rheumatic fever is a periarteritis, accompanied by increased permeability of the vessel wall. It may occur in the lung as elsewhere throughout the body.

4. *Obliteration of Vessels by Adjacent Disease.*

Tuberculosis.

Many acute and chronic pneumonias produce vascular occlusion which hinders natural body defenses and prevents repair.[4] This is best illustrated by a study of the vascular system of excised lungs after injection of the vessels with radiopaque material as Birkelo and Brosius have shown (Fig. 5, *a* and *b*). When attention is centered upon the pulmonary consolidation occurring in most diseases of the lung, the degree of vascular damage is often overlooked.

5. *Hypersensitivity States.*

Periarteritis nodosa.

CASE V. B. S., male, white, aged forty-five,

hospitalized because of rapid loss of 30 lb. in weight, severe pains in all extremities, asthmatic attacks, and asthenia. Found to have a basal metabolic rate of plus 50 per cent and gallstones. Initial diagnosis was hyperthyroidism and peripheral neuritis due to avitaminosis. Developed several attacks of sudden respiratory embarrassment with cyanosis requiring oxygen, in one of which death ensued. Admission roentgenogram, July 15, 1939, showed nothing abnormal in the chest (Fig. 6*a*). During a sudden attack of extreme respiratory distress on August 4, 1939, extensive changes were seen in the inner two-thirds of each lung field compatible with edema due to increased capillary permeability (Fig. 6*b*). No evidence of heart failure was present. Symptoms ceased abruptly after forty-eight hours and the follow-up roentgenogram on August 14, 1939, showed remarkable clearing of the shadows (Fig. 6*c*).

Comment. The pulmonary manifestations of periarteritis nodosa are mentioned infrequently.[7] These patients all have a long history of "asthmatic" attacks which are probably transient episodes of pulmonary edema, progressively severe, and ending in respiratory failure. It is not widely realized that subacute or chronic states resembling periarteritis nodosa may exist, and that a mild form of the disease may occur in epidemic form.[5]

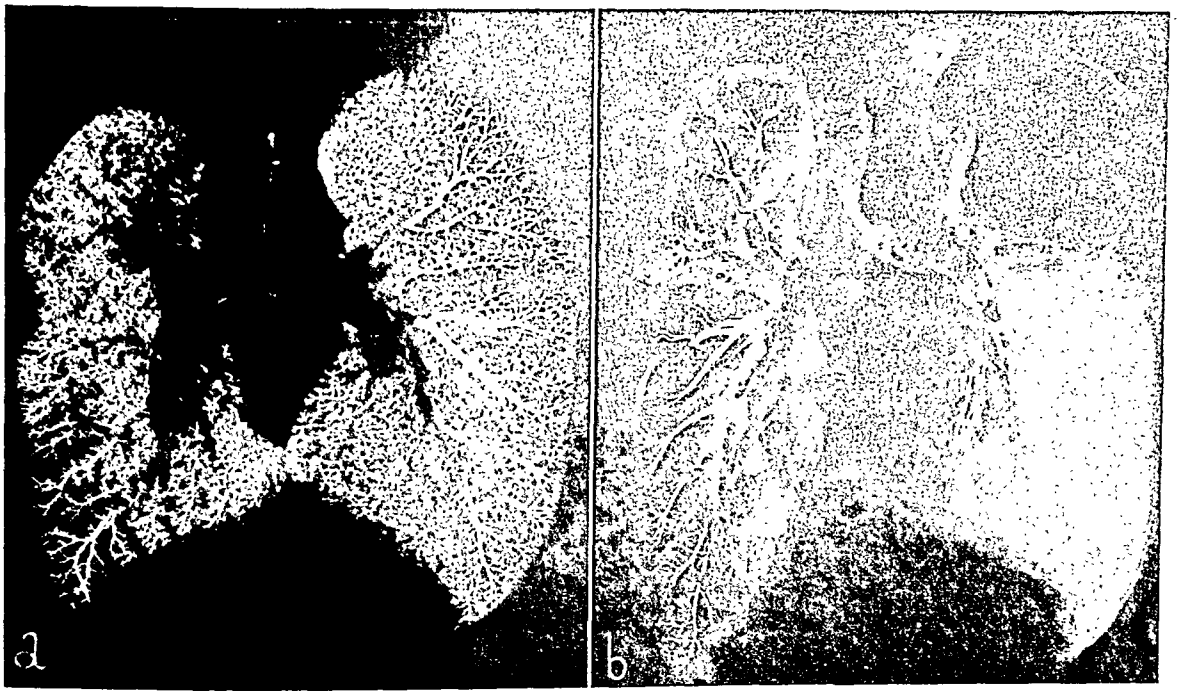


Fig. 5. (Kindness of Drs. Birkelo and Brosius.) *a*, roentgenogram of excised normal lungs after injection of the vascular system with opaque material. Note the lacy pattern and the extensive ramifications of the small vessels at the pleural surfaces. *b*, roentgenogram of excised tuberculous lungs under similar conditions. Note the marked reduction in vascularity of the right lung in particular. It is thought that this degree of impairment of blood supply is an important factor in preventing healing of the disease.

CONCLUSION

Reference to Table 1 will indicate the diversity and extent of the pathology touched upon in this paper. There has been presented an illustration, with explanatory notes, of each of the main headings in the table. By this means it is hoped to advance a new point of view in regard to vascular lesions in the lungs which may be useful in the differential diagnosis of many otherwise obscure clinical conditions.*

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* For discussion see page 37.

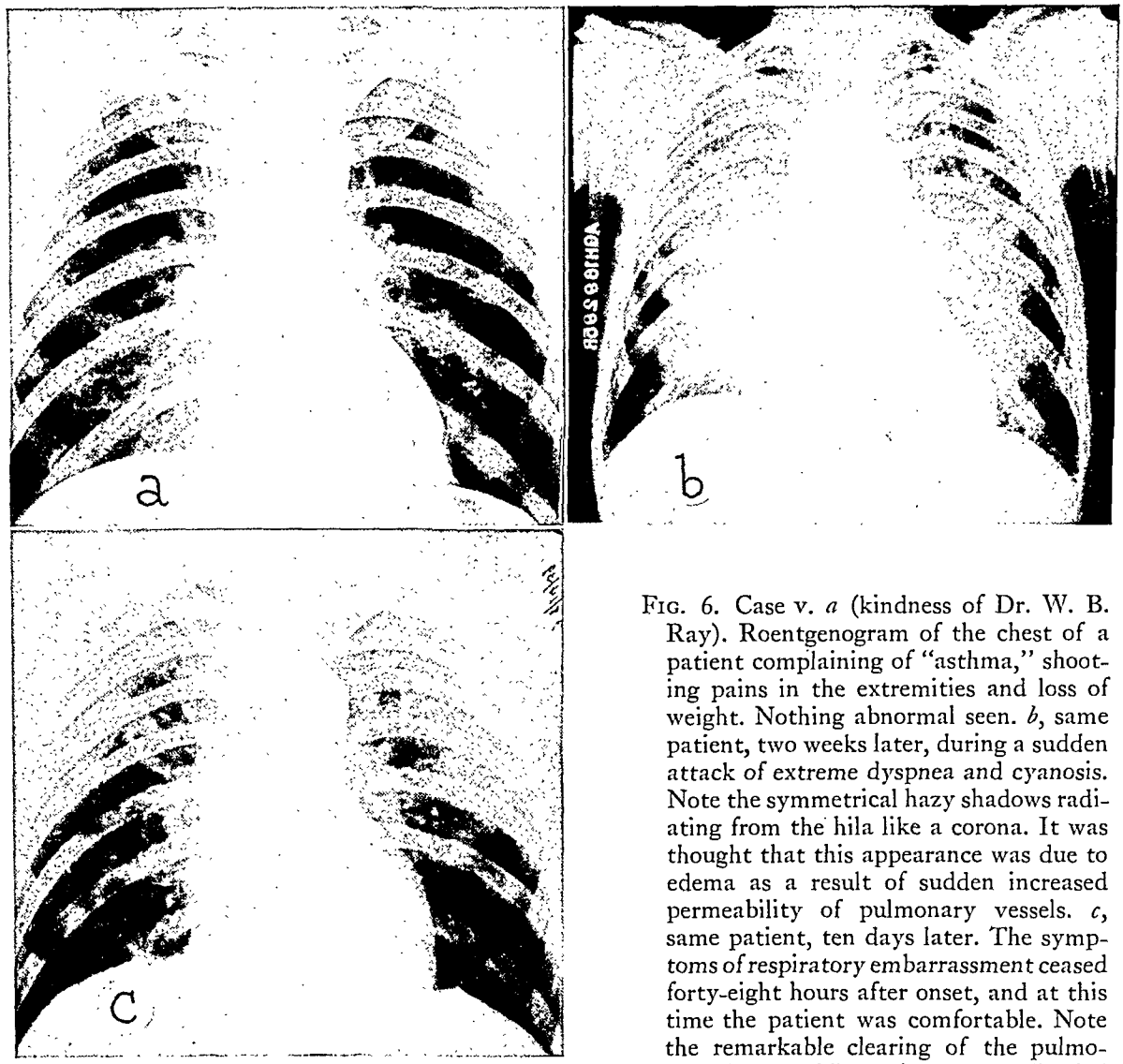


FIG. 6. Case v. *a* (kindness of Dr. W. B. Ray). Roentgenogram of the chest of a patient complaining of "asthma," shooting pains in the extremities and loss of weight. Nothing abnormal seen. *b*, same patient, two weeks later, during a sudden attack of extreme dyspnea and cyanosis. Note the symmetrical hazy shadows radiating from the hila like a corona. It was thought that this appearance was due to edema as a result of sudden increased permeability of pulmonary vessels. *c*, same patient, ten days later. The symptoms of respiratory embarrassment ceased forty-eight hours after onset, and at this time the patient was comfortable. Note the remarkable clearing of the pulmonary shadows. The patient eventually died and postmortem examination showed periarteritis nodosa.

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LUNG FUNCTION*

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MEDICINE has passed beyond the stage of descriptions of disease entities, of purely anatomic considerations and postmortem reconstructions, of qualitative estimates of function, into the stage of accurate quantitative measurements of the changes which disease imposes on the living body. As part of this symposium on the lesser circulation there follows a brief review of some of the common methods of estimating pulmonary function and of some of the more recent methods which have been developed.

The oxygenation of the blood and the removal of its carbon dioxide are functions of the lungs which normally, even during moderate exercise, are accomplished without the occurrence of dyspnea or discomfort. One of the earliest symptoms of cardiorespiratory dysfunction is the appearance of dyspnea during slight exertion, a symptom which the patient himself notices. The patient, however, cannot evaluate objectively the degree of disability. It is for this reason that various methods have been developed to measure the function of the lungs. These methods may be divided into four main groups:

1. Static measurements of the volume of the lungs include the determination of vital capacity, total lung volume, and functional residual air.

Vital capacity is determined in the ordinary manner. Residual air is that volume of air remaining in the lungs after a maximum expiration. In man residual air is measured by indirect methods such as the dilution technique, in which the subject breathes 100 per cent oxygen in order to eliminate most of the nitrogen from the lungs. If the initial proportion of nitrogen in the lungs is known and the volume of nitrogen eliminated is measured, the total lung volume can be calculated. By subtracting the vital capacity from the total lung volume the volume of residual air is obtained.

These relatively simple methods can supply important information regarding pulmonary abnormalities. For example, in emphysema the (functional) residual air is increased to almost one-half of the total lung volume. Such a proportion of residual air results in a very definite change in respiratory function due to inadequate mixing of the inspired air.

There has recently been developed an apparatus for the continuous determination of the nitrogen content of a gas mixture. This instrument contains an evacuated tube into which is sucked the gas to be studied and through which is passed a 2,000 volt current. In the presence of nitrogen a characteristic color is produced which is more intense the more nitrogen is present. The principle is similar to that of ordinary neon signs. Using this device to analyze continuously the nitrogen content of the expired air, one is able to obtain within a few seconds data which formerly were acquired much more laboriously. It is thus now possible to determine in large groups of individuals of all ages the normal volumes of dead space, tidal air, residual air, and total lung volume, and to test similar large groups of individuals having impaired respiratory function.

2. The second group of methods might well be called dynamic ventilation tests. The rate, the depth, the minute volume of respiration, and other factors can be measured in relation to rest and exercise.

The maximum breathing capacity can be measured by having the subject breathe into a spirometer for thirty seconds as rapidly and deeply as possible. Some physi-

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cally fit individuals can breathe as much as 175 liters of air per minute. If the normal maximum breathing capacity is known for an individual, a subsequent reduction of this capacity signifies a diminished pulmonary reserve.

The velocity of air flow in the trachea can be measured by exposing to the air flow a wire so fine that it will be deflected by the velocities usually present. The amount of deflection can be measured and recorded. Another instrument for measuring such velocities consists of a fine wire mesh with manometers on either side. The passage of air through this instrument sets up a differential pressure gradient which increases with the velocity of the flow. Measurements of this sort are essential in the development of equipment for oxygen therapy. It is not generally recognized that a dyspneic individual whose minute volume of respiration is 20 liters must at the peak of inspiration move air at the rate of 60 liters a minute. If oxygen cannot be delivered at this high rate the patient will be inadequately supplied with oxygen for a short period during every inspiration. Since such velocity determinations give some indication of an individual's ability to expel material from the respiratory tact, they are also of interest in patients with atelectasis, pneumonia and fibrosis.

In a certain proportion of normal subjects, the inspired air will be unequally distributed between the various lobes of the lung with the result that the oxygen saturation of the blood leaving a lobe will vary depending upon the degree of efficiency of ventilation in that lobe. Such inequality in the distribution of inspired air is more often found in patients with pulmonary disease in which secretions or other obstructions may bar access to some alveoli. The degree of mixing in the lung can be measured by determining the amount of nitrogen in a sample of the alveolar air of a patient who has breathed 100 per cent oxygen for seven minutes. Normally at the end of seven minutes of breathing pure oxygen the nitrogen will be less than 2 per cent of the alveolar air. In patients who have unequal lung mixing due to emphysema the sample of alveolar air may contain 5 or 7 per cent of nitrogen.

3. Another group of measurements are concerned with the diffusion of gases between the alveoli and the blood. The arterial blood can be analyzed for its pH and for its oxygen and carbon dioxide content. From such data the tension or pressure of the gases in the blood leaving the lungs can be calculated. Direct measurements of the tension also can be made but the technique is complicated and time consuming.

Since it is the pressure of the oxygen in the plasma which drives the oxygen molecules into the tissue cells, a knowledge of the tension of oxygen in the arterial blood is of more importance in determining the degree of anoxemia than a knowledge of the percentage oxygen saturation of the hemoglobin. Yet clinicians are usually content to estimate the degree of anoxemia by the oxygen saturation of the hemoglobin or by the cyanosis which the patient may exhibit. Unfortunately, cyanosis is rarely apparent until the oxygen in the hemoglobin has fallen from a normal value of 97 per cent to 85 or 80 per cent (at which point the tension of oxygen in the blood may have fallen from the normal of 100 mm. of mercury to 70 mm.), and a considerable reduction of the tension of oxygen can occur before any perceptible decrease in oxygen saturation can be detected by chemical examination. This latter fact is made possible by the peculiar ability of hemoglobin to retain oxygen, as illustrated by the shape of the oxygen dissociation curve of hemoglobin. Therefore, although a decrease in the saturation of hemoglobin with oxygen indicates that the diffusion of oxyen in the lung is inadequate, the tension of the oxygen in the arterial blood is a better guide because it is more sensitive and is altered sooner in disease.

It should be noted that a normal tension of oxygen and of carbon dioxide can be present in the blood even though a lung may have suffered considerable anatomic

damage. For example, if a disease process, such as a large lung cyst, has shut off the blood supply to the affected area of the lung, leaving the remainder of the lung normal, the blood passing through the lung will not be subjected to abnormalities of diffusion and therefore studies of the gases of the blood will be normal, although roentgenologic examination would reveal the abnormality.

4. The last group of measurements are more concerned with pulmonary blood flow. They include measurements of pulmonary circulation time, of the pressure in the right ventricle and in the pulmonary artery, of the volume of the pulmonary blood, and of the cardiac output.

The speed of the pulmonary circulation can be determined by a relatively new device, the oximeter, which when placed on a patient's ear will record the degree of saturation of the hemoglobin by means of a photoelectric cell. As the hemoglobin becomes increasingly saturated and therefore redder in color, more light is transmitted to the photoelectric cell thereby increasing its output of electrical current. If 100 per cent oxygen is breathed, the oximeter will, by increasing its electrical output, show a distinct increase in the saturation of the hemoglobin within five to seven seconds. This is the shortest time in which the excessively oxygenated blood can get from the lungs to the ear. Any delay in this response of the oximeter indicates either a slow circulation through the lungs or the presence of rather uniform and widespread pulmonary lesions such as bilateral pulmonary edema, emphysema, or fibrosis.

Since the techniques of catheterization of the heart are discussed elsewhere in this symposium, that phase of lung function will not be taken up here.

The methods already outlined, dealing with the lungs as a whole, do not distinguish between the function of the right and left lungs. Some of these tests can be performed upon the two lungs separately by the technique of bronchospirometry or catheterization of the individual lungs. Since in these circumstances the breathing is markedly altered, the data obtained cannot with assurance be analyzed quantitatively.

The methods outlined here have been developed through the cooperation of the physicists and chemists who designed the instruments, the physiologists who specified what the instruments should measure and the clinicians whose task will be to apply these new methods to the study of disease. The ability to make accurate measurements easily should prove to be a stimulus to the study of pulmonary function.*

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* For discussion see page 37.

CONDITIONS WHICH RESULT IN INCREASED PRESSURE WITHIN THE LESSER CIRCULATION*

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HYPERTENSION within the lesser circulation may arise under a variety of circumstances. Until the recent development of the procedure for catheterization of the heart, there was no practical method for measuring the pressure in the pulmonary circuit. Recognition of pulmonary hypertension depended, therefore, on a knowledge of the various mechanisms capable of producing it and on the recognition of the secondary phenomena resulting from its presence. Although new knowledge concerning pulmonary hypertension undoubtedly will be disclosed by catheterization, it is well to review the information which can be gained without resorting to this procedure.

Any mechanism which leads to increased pressure in the lesser circulation increases the work of the right ventricle. If this increased pressure persists, hypertrophy of the right ventricle results. Arteriosclerotic changes in the pulmonary arteries follow and over a period of time, when the reserves are exhausted, failure of the right side of the heart ensues. In certain conditions in which rapid development of pulmonary hypertension occurs, dilatation rather than hypertrophy of the right ventricle takes place. This change is reversible if the cause of the increased pressure is eliminated.

The signs of pulmonary hypertension which are disclosed to the roentgenologist are (1) enlargement of the pulmonary arteries and of the outflow tract of the right ventricle (conus) and (2) enlargement of the right side of the heart. If incompetence of the pulmonary valve is added because of dilatation of the right ventricle, the phenomenon of "hilar dance," an exaggerated pulsation of the pulmonary arteries in the hilus of the lung, also may be seen.

The sign which is present earliest is enlargement of the pulmonary artery and of the outflow tract of the right ventricle, the pulmonary conus. Usually the enlarged pulmonary conus can be seen as a convexity of the upper portion of the left border of the cardiac silhouette. In the right anterior oblique position this convexity is more marked and this portion of the heart shadow may bulge into the retrosternal space.

In addition to enlargement of the conus the branches of the pulmonary artery in the hilus of the lung may appear dilated. Schwedel stated that the descending branch of the right pulmonary artery normally measures between 9 and 14 mm. in diameter. These figures apply only if teleroentgenograms are employed and the artery is measured in its upper portion perpendicular to the bronchus which defines its medial border.

Enlargement of the right ventricle usually appears on the posteroanterior roentgenogram of the thorax as enlargement of the heart shadow to the left. The diaphragmatic segment of the heart is found, in the left anterior oblique position, to be increased in size and its ventral border is rounded. Enlargement of the left ventricle will, in this position, produce a rounding of

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the dorsal border of the cardiac shadow. As enlargement progresses the tricuspid valve may become incompetent and the right auricle may become dilated; this produces enlargement of the heart shadow to the right.

In a typical case the roentgenologist will see a convex left border of the heart possibly with some enlargement of the cardiac silhouette. The aortic knob may be less prominent than usual because of rotation of the heart on its vertical axis, and the hilar vessels may be dilated.

CAUSES OF PULMONARY HYPERTENSION

The various conditions which cause pulmonary hypertension may be classified into the following groups:[5] (1) obstruction to the lesser circulation beyond the pulmonary circuit, (2) obstruction within the pulmonary system, (3) abnormal shunts of blood from the arterial side into the pulmonary circulation and (4) kyphoscoliosis.

Obstruction beyond the Pulmonary System. The two most common causes of pulmonary hypertension due to obstruction beyond the pulmonary system are mitral stenosis and a failing left ventricle for any cause. In either instance the vessels of the lesser circulation are overloaded and the efferent blood stream from the lungs is impeded. In some cases of mitral stenosis arteriosclerotic changes develop in the arterioles of the lesser circulation,[8] which further adds to the burden placed on the right side of the heart.

In addition to the enlargement of the conus, as seen on the roentgenogram, mitral stenosis produces enlargement of the left auricle. This can best be demonstrated roentgenologically by the posterior displacement of the barium-filled esophagus with the patient in the right anterior oblique position.

Obstruction within the Pulmonary System. Within the pulmonary circuit the lesser circulation may be obstructed at different levels. The main pulmonary vessels may be occluded by an embolus or a thrombotic process.[7] The small and medium-sized branches of the pulmonary arterial tree may become occluded in the course of sickle cell anemia,[13] schistosomiasis[3] or extensive metastatic carcinomatosis.[2] The pulmonary arterioles may become sclerotic[6] or they may undergo obliterative changes in association with many pulmonary diseases. Finally, the capillary system may be obstructed in emphysema and in widespread pulmonary fibrosis[10] such as that found in tuberculosis and pneumoconiosis.

Shunts. Abnormal shunts of blood from the arterial side into the lesser circulation are usually congenital but may be acquired. The most common congenital lesions of this type are patent ductus arteriosus, interatrial septal defect and Lutembacher's syndrome (interatrial septal defect and mitral stenosis). Rarely a shunt may be acquired by the gradual rupture of an aortic aneurysm into the pulmonary artery.[4]

Kyphoscoliosis. Kyphoscoliosis probably causes pulmonary hypertension because the thoracic deformity produces areas of atelectasis and of emphysema in the lung. It is a well known fact that most hunchbacks die of heart failure. Bachmann has shown that in 87 out of 154 cases death was due to failure of the right side of the heart.

A condition which produces pulmonary hypertension and one in which an early roentgenologic diagnosis is often extremely important is pulmonary embolism. In many cases of pulmonary embolism the clinical features are so typical that roentgenologic aid is unnecessary. In others, particularly in those in which the clinical features are minimal or misleading, the roentgenologic signs may be of inestimable aid in arriving at a proper diagnosis.

Westermark has stated that the roentgenologic sign of pulmonary embolism unaccompanied by infarction is a decreased density of the segment of lung supplied by the occluded artery. This appearance is due, he has said, to the lack of blood in that portion of the pulmonary arterial tree.

In many instances the roentgenologist may see the signs of acute cor pulmonale[12] (Fig. 1). These are dilated pulmonary ves-

sels in the hilus, enlarged conus shadow and enlarged heart. It is probable that the sudden change in pressure in the lesser circulation is due to generalized spasm of the arterioles of the lung as well as to occlusion of a larger vessel. At any rate, if the patient survives, canalization of the occluded artery takes place and the pulmonary hypertension subsides. Eventually the heart and pulmonary vessels return to normal size.



FIG. 1. *a*. Before operation. The size and shape of the heart and pulmonary arteries are normal. *b*. Fourteen days after cholecystectomy and one day after the onset of pain in the right side of the thorax. Signs of acute cor pulmonale are seen in the dilated pulmonary arteries, enlarged heart and convex upper segment of the left border of the cardiac shadow. The patient died a few hours after this roentgenogram was made. An embolus in the right pulmonary artery was found at necropsy.

It is well to point out here that a roentgenologic diagnosis of pulmonary embolism based on the signs of pulmonary hypertension is often possible before the roentgenologic signs of pulmonary infarction and of pleural reaction appear. In such cases therapeutic measures can be instituted earlier, a feature which may save the life of the patient.

SUMMARY AND CONCLUSIONS

Pulmonary hypertension is a secondary manifestation of a wide varitey of conditions which exert their effects either by obstruction of the lesser circulation in or beyond the pulmonary circuit, or by shunts of arterial blood into the pulmonary circulation. Regardless of the mechanism responsible for its production, pulmonary hypertension is recognized by the secondary effects on the cardiorespiratory system eventuating in right ventricular hypertrophy or dilatation, changes characterized roentgenologically by enlargement of the pulmonary artery and conus. Absence of enlargement of the left auricle is evidence that the obstruction is within the pulmonary circuit.

Early diagnosis of pulmonary embolism, especially in those cases in which minimal or misleading clinical features occur, is possible by the recognition of the roentgenologic signs of acute cor pulmonale.*

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* For discussion see page 37.

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THE EVALUATION OF THE LESSER CIRCULATION AS PORTRAYED BY THE ROENTGENOGRAM

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THE lesser circulation is one of the last of the major systems to yield to exploration and evaluation by means of the roentgen examination. The lesser circulation is unique in that it is completely enclosed within the thorax and therefore is very difficult to explore by direct observation. There has been considerable controversy as to who is entitled to the credit for the first description of the lesser circulation. Some historians contend that Servetus, Realdus Columbus or Ibn Nafis was each the discoverer of the lesser circulation. However that may be, very little was contributed to our knowledge of the lesser circulation until the latter part of the Nineteenth Century. Until the last few years, the investigation of the lesser circulation has been done by physiologists and by animal experimentation. These researches were very ingenious and were carried on by many investigators in the various fields of anatomy and experimental physiology. It is most interesting to find that the present day direct investigation of the lesser circulation has proved the accuracy of the physiologist.

The final evaluation of the lesser circulation by means of the roentgen examination is dependent upon the correct portrayal of the anatomy of the chest, its physiological and mechanical variations and the various disease conditions which may be present. The portrayal of the anatomy of the lungs and heart is dependent upon the air content of the lungs. Without air in the lungs, there is no differentiation of the anatomical structures. When the lungs are well inflated, the anatomical structures are visualized, both as to size and position and character, by the displacement of the air content. The pathologic conditions must disturb the normal position or relationship of the air within the thorax in order to reveal their presence and character. Therefore, full inspiration is very essential in the making of the roentgenogram of the chest. This is not always easy, as frequently inspiration is not complete and may be confusing in the study of the air content in the lungs (Fig. 1). Again, expiration may be utilized to demonstrate the presence of emphysema as noted by Westermark.[1] The total lung capacity is twenty times that necessary for aeration of the blood during periods of rest.[2] Also, there is a definite relationship between the air content of the lungs and the blood volume.[3] Without motion, there is no lymphatic flow within the lungs, and it is necessary that any free fluid, either blood or lymph, be outside the blood or lymph vessels and in the air sacs or bronchi where it will interfere with the presence of the air content in order that it may be demonstrated by the roentgen ray. Hemorrhage or lymph stasis sufficient to involve the interstitial framework of the lung also involves the air sacs. Aneurysms of the arteries or veins may be demonstrated by their size.

The technical factors in the making of the roentgenogram of the chest are quite important. This is particularly true in the study of the lesser circulation where the highest quality of definition and contrast is necessary. If the film is not exposed in one-twentieth of a second or less, motion of the heart and vessels will interfere with the sharpness of the delineation on the film.[4] Likewise, underexposures or overexposures

[1] Westermark, N. On bronchostenosis; a roentgenological study. *Acta radiol.*, 1938, *19*, 285–336.

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* Presented at the Forty-eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16–19, 1947.

may reveal too much or too little of the anatomy of the lungs. No one position is adequate for the portrayal of the various anatomical structures, but, rather, many different positions are necessary, dependent upon the disease condition to be studied. The required position will tax the ingenuity of the roentgenologist.

A detailed knowledge of the mechanical and physiological variations of the lungs discuss the presence or absence of pulmonary fibrosis—a most difficult problem in the evaluation of the lesser circulation. Such a study will often raise the question as to when in the human life cycle disease actually begins. This may be very important to the patient with beginning pulmonary fibrosis which will culminate in cor pulmonale. If the roentgenologist is to be of the greatest value to the clinician then,

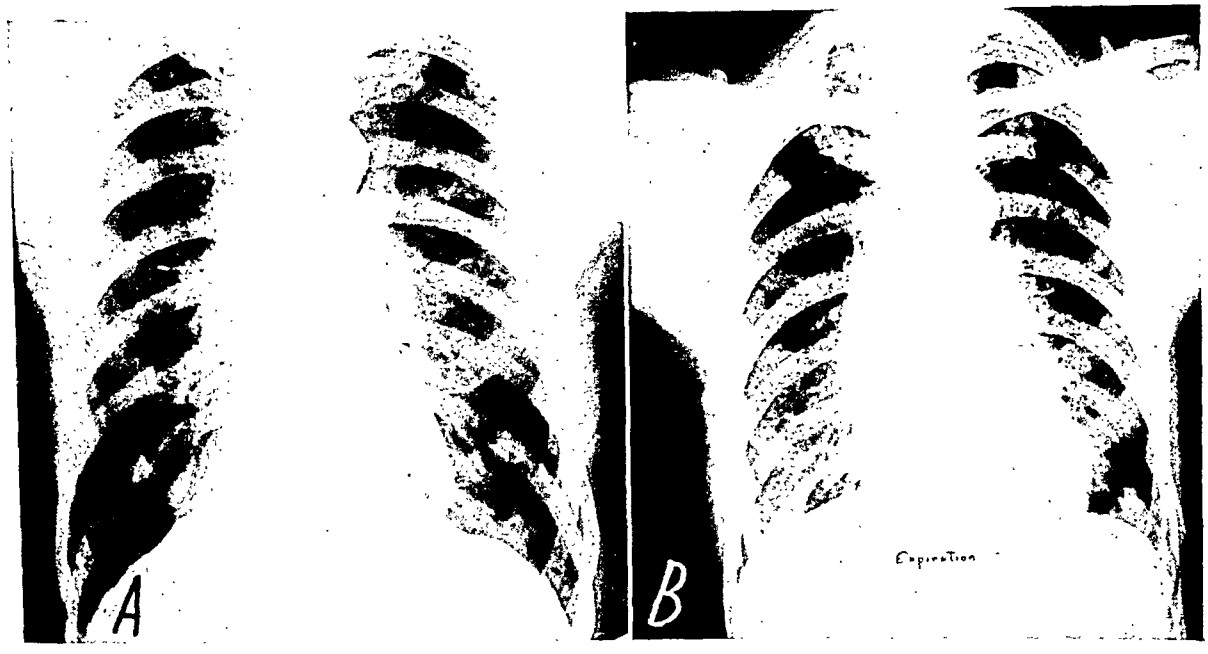


Fig. 1. *A*, complete inspiration; *B*, incomplete inspiration. Illustrating different phases of inspiration which may simulate increased bronchial and arterial densities resembling increased fibrosis.

and heart is most essential for the study of the lesser circulation. The infant is born with a certain anatomy, but physiological changes take place very rapidly in the blood flow through the pulmonary vessels,[5] the air content of the lungs, and the relative connective tissue content of the lungs. This connective tissue content of the lungs changes according to the various age periods of life and is influenced by many disease conditions. Such knowledge of the connective tissue content of the lungs at various age periods of life should be had so that the roentgenologist may accurately he must be able to foresee that certain conditions of the lungs and heart, as portrayed by the roentgenogram, may lead to serious complications. Serial examinations over a period of months and years not only yield much general scientific information as to the beginning and progress of disease,[4] but will often be of the greatest value to the patient. The heart volume is not a constant factor but will vary according to the general health of the patient as well as to the blood volume and its pressure.

It has been stated that a demonstration of enlargement of the right ventricle is necessary for the diagnosis of increased

[5] Wasson, W. W. Roentgenographic study of the infant chest as seen at birth. *J.A.M.A.*, 1924, *83*, 1240–1242.

tension within the lesser circulation.[6] Unfortunately, such dilatation of the right heart is a late stage in any disease affecting the lesser circulation, and the goal of the roentgenologist and clinician should be to foresee the possibility of such a dilatation and, wherever possible, to prevent its occurrence. As to whether a dilatation of the right heart will or will not occur is dependent upon whether or not the balance of the

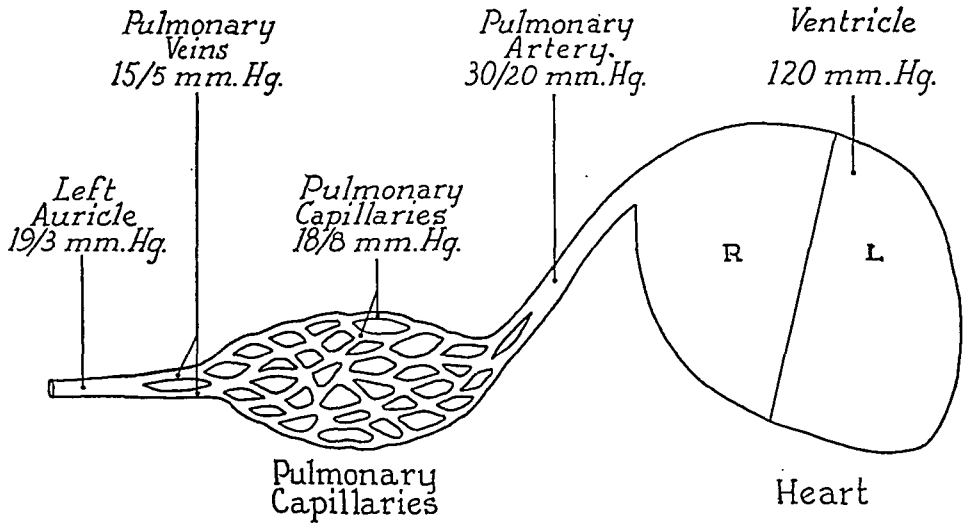


FIG. 2. Diagrammatic representation of the pressure gradient in the lesser circulation.

mechanical and physiological factors which control the flow of blood through the lungs is sufficiently disturbed. If the clinician or roentgenologist is to have an appreciation of the delicate balance which exists between the flow of blood within the capillaries, the lymphatic flow within the lymph vessels and the to-and-fro movement of the air columns within the bronchi and air sacs, he must be familiar with the circulatory changes which take place at birth, together with the pressure gradient within the pulmonary vessels and the intrapulmonary air pressures (Fig. 2). No satisfactory explanation has yet been presented as to why the blood pressure within the pulmonary vessels drops so rapidly after the first inspiration and maintains such a low pressure as one-fifth to one-sixth that of the greater circulation throughout life. Unquestionably, the intrapulmonary air pressures which change with each inspiration and expiration influence the flow of blood not only through the great veins, but likewise through the pulmonary capillaries[2] (Fig. 3). The pulmonary capillaries lying naked to the air columns within the air sacs[7] must be very sensitive to the changing air pressures. Under normal living conditions, the thickness of the right ventricular wall does not increase after birth, while the thickness of the left ventricular wall increases to two or three times the thickness of the right ventricular wall[2] (Fig. 4). It would therefore seem that there must be another great force other than the propelling power of the right heart which aids in the movement of the great volume of blood through the lungs. Consequently, the thickness of the right ventricular wall and its ratio to the left ventricular wall may be used to calculate the probable pressure in

[6] Schwedel, J. B. Clinical Roentgenology of the Heart. Ann. Roentgenol. Vol. 18, Paul B. Hoeber, New York, 1946.

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the lesser circulation if the blood pressure in the greater circulation is known.[2] The demonstration of an enlargement of the right heart by means of the roentgenogram is necessary for a definite statement that there is increased pressure within the lesser circulation, as so many times there appear to be pathological changes within the chest which should increase pressures within the lesser circulation, and yet no such increase exists. Such a demonstration by the roentgenogram is often not easy. With enlargement of the right side of the heart the heart may rotate so that in the posteroanterior view, the heart borders may appear quite normal (Fig. 5). On the other hand, lateral and oblique views of the heart may reveal definite enlargement of the right ventricle, the right auricle and the pulmonary conus and artery.

Until quite recently, the portrayal upon the roentgen film of the heart and the lesser circulation depended upon direct visualization of these structures upon the roentgen film and by a contrast medium in the bronchi or the esophagus. As a basis for his evaluation of the lesser circulation as portrayed upon such roentgen films, the roentgenologist had access to the research of many anatomists, physiologists and surgeons. There was one report of the study of the blood pressures within the pulmonary arteries as found at the time of

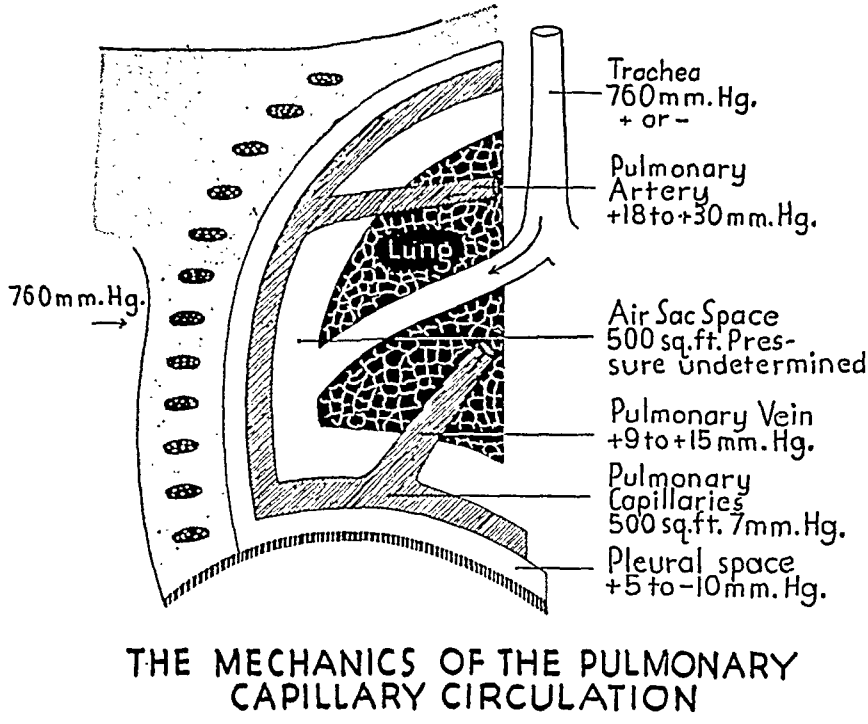


Fig. 3. Sketch illustrating intrapulmonary air pressures, the pulmonary artery, capillary and venous pressures, and the pumping action of inspiration and expiration.

THICKNESS OF VENTRICULAR WALLS AT VARIOUS AGE PERIODS

Age	Left	Right
Birth	*4-4.5mm.** *0.3cm.***	*3-4mm.** *0.3-0.5cm.***
1 year	*2X right**	
Puberty	*3X right**	
Adult	*1.5-2cm*** *10-15mm****	*0.5-0.7cm*** *5mm****

* Abt's Pediatrics, 1924
** Pathological Technique, F.B. Mallory, 1938
*** A Text-book of Pathology, Wm. Boyd, 1938

Fig. 4. A chart showing the relative thickness of the right and left ventricular walls at various ages.

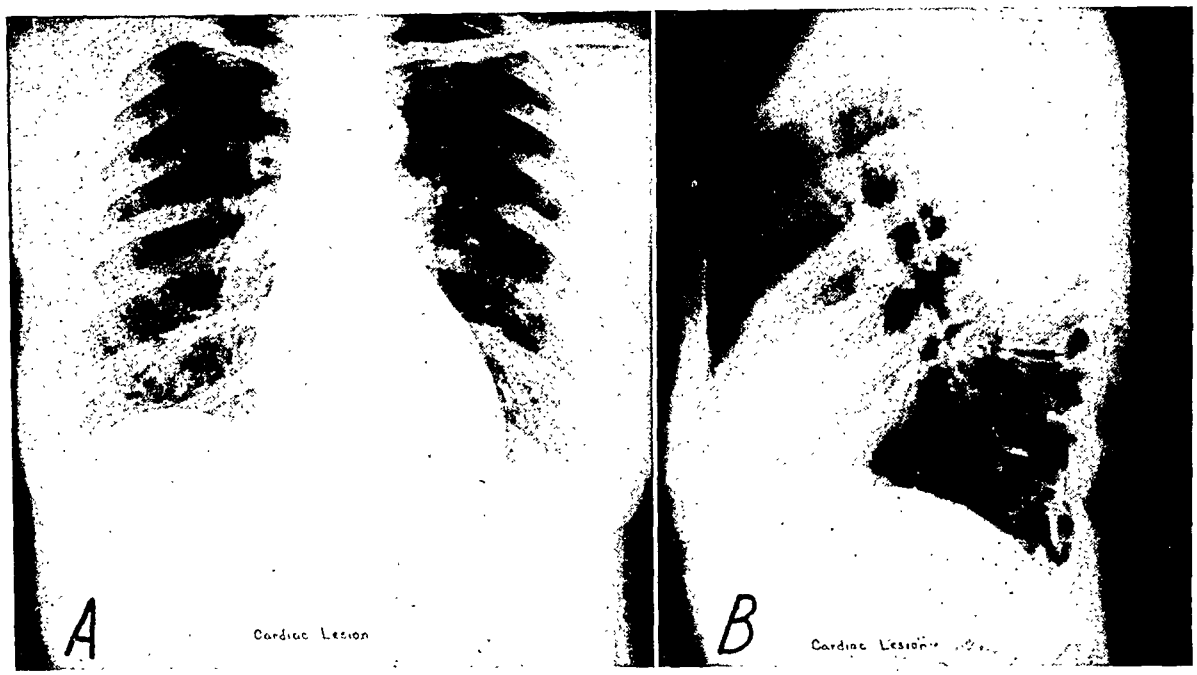


FIG. 5. *A*, heart with normal appearing contours. *B*, same patient, lateral view, full inspiration with diaphragms well down, no kyphosis, but with the lower trachea and bronchi pushed posteriorly by a rotation of the heart with increased diameters; therefore, no shortening of the superior-inferior diameter. A shortening of the superior-inferior diameter from any cause can also produce this appearance.

operation.[8] The determination was made by means of needle puncture. Forssmann's catheterization of the right side of the heart[9] was utilized and elaborated by Cournand and his co-workers[10] who studied the circulation by inserting an x-ray catheter through the veins of the arm and chest and into the right auricle. Their studies stimulated similar investigations by many others. They yielded most valuable data concerning the blood pressure of the lesser circulation and have laid the basis for the surgical correction of many of the congenital heart conditions. Thorotrast has been used for the study of the heart, the great vessels, the pulmonary arteries and veins, and it has enabled the roentgenologist to differentiate aneurysms of the pulmonary vessels and arteriovenous fistulae from other confusing tumors of the lung. Some most interesting arteriovenous fistulae and aneurysms have been reported.[6,11]

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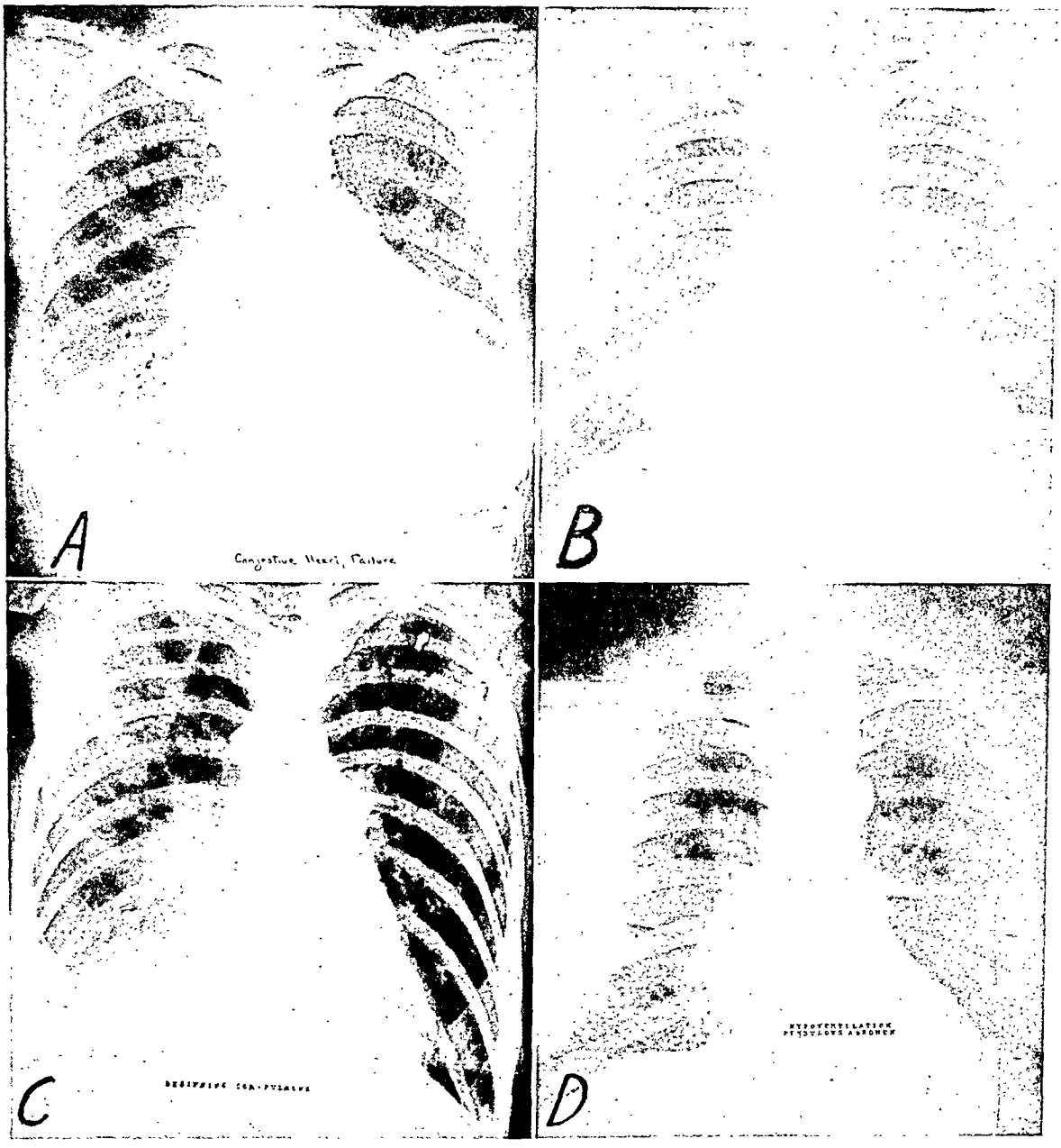


Fig. 6. Four cases illustrating four major classes of disease of the lesser circulation.

A, congestive heart failure; illustrating diseases of the heart, Class 1.

B, arteriovenous fistula (courtesy of Doctors Lawrence and Kerby) illustrating primary disease of the pulmonary vessels, Class 2.

C, cor pulmonale; illustrating diseases of the lungs involving the lesser circulation, Class 3.

D, obesity with hypoventilation; illustrating abnormalities of the thorax influencing the lesser circulation, Class 4.

Another aid in the differential diagnosis is the study of the pulmonary arteries in either lung. Frequently, under pressure the branches of the pulmonary arteries in the lung roots will become dilated and will pulsate to give what has been termed "hilar dance."[6] The pulmonary arteries in the body of either lung may also become prominent and in serial study will give the suggestion of probable increased pressure within the lesser circulation. Finally, there is the lymph stasis or edema of the air sacs

which displaces the air within the air sacs and is readily shown upon the roentgenogram. Such a sign is very characteristic of increased pressure within the lesser circulation and increased permeability of the capillaries or of lymph stasis from any cause. This finding, however, is always associated with atelectasis and many times it is difficult to determine which condition predominates: atelectasis, lymph stasis, or capillary congestion.

A recheck of the list of diseases of the chest and the lesser circulation reveals the fact that there may be a few diseases which are primary to the lesser circulation, but that most of the diseases of the lesser circulation are secondary to other diseases of the chest. In fact, all diseases of the chest may involve the lesser circulation more or less, and even diseases of the greater circulation quite distant from the chest may produce secondary involvement of the lesser circulation. In order to further differentiate and diagnose the diseases of the lesser circulation, it is necessary that some classification be attempted. It seems that there may be four great classes of diseases of the lesser circulation:

1. Disease of the heart, which may be either primary or secondary. It is quite evident that the disease of the heart will be distinctive, clinically or roentgenographically, either as a congenital anomaly or as an involvement in later life. Such disease of the heart may be either primary or secondary and will interfere with the propelling power of the blood through the lesser circulation, as in the congenital anomalies, valvular disease or congestive heart failure, and so forth (Fig. 6*A*).

2. There are a few diseases of the pulmonary arteries and veins which are primary, and which are quite characteristic as a class when viewed roentgenographically: primary sclerosis of the arteries, aneurysms, arteriovenous fistulae and rheumatism. There are also involvements which are secondary to disease elsewhere in the body and which are also characteristic as a class, such as emboli, metastatic tumors, allergic response, and so forth (Fig. 6*B*).

3. There is that group of diseases of the lungs which may involve the lesser circulation secondarily by either interfering with the passage of blood through the pulmonary vessels by pressure or constricting these vessels, as in pulmonary fibrosis, or by direct inflammatory involvement of these vessels, as in pulmonary tuberculosis. This large group is then characterized by those extensive diseases of the lungs producing pulmonary fibrosis, ulceration, and so forth, and result in increased pressure within the lesser circulation and dilatation of the right heart. This final stage has been termed cor pulmonale. Ayerza's disease is considered as cor pulmonale, by most writers[11a,12] (Fig. 6*C*).

4. Finally, there is that group of diseases of the chest which may indirectly influence the lesser circulation by disturbing especially the mechanics of the chest, such as deformities of the chest, obesity, kyphosis of the thoracic spine, the funnel chest, and other anomalies of the thoracic cage which affect the lesser circulation by displacing the viscera or by interference with the correct ventilation of the lungs. Similarly, obesity as described by Kerr[13] will interfere with the proper diaphragmatic action, and therefore interfere with adequate ventilation of the lungs. Such interference with inspiration and expiration and the loss of this power of propelling the blood will throw increased strain upon the right heart, and many of these patients will have cardiac distress. The postoperative fixation of the diaphragms and the resulting hypoventilation of the lung bases, and again increased strain upon the right heart belong in this general class. Trauma of the chest wall with fixation of the chest will produce similar conditions of hypoventilation and increased strain upon the right heart (Fig. 6*D*).

SUMMARY

This paper has endeavored to present the following points:

1. The necessity of complete aeration of the lungs for portrayal of the anatomy of the lesser circulation.

2. The importance of utilizing the correct technical factors in the portrayal of the lesser circulation by means of the roentgenogram.

3. The necessity of a knowledge of the

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physiology and mechanics of the lesser circulation, and the beginnings of diseases for the evaluation of the right heart and increased pressures within the lesser circulation.

4. Four general patterns of disease of the lesser circulation are presented.

DISCUSSION OF SYMPOSIUM ON THE LESSER CIRCULATION*

Dr. Wendell G. Scott, St. Louis, Mo. Six years ago in December, 1941, Dr. Wasson conducted the first symposium on the lesser circulation at the meeting of the Radiological Society in San Francisco. At the conclusion of that symposium, the discussion was opened by Dr. W. E. Chamberlain, and from the presentations he said, "We have had a fine discussion of the gross anatomy and of the basic problems in pathology and physiology. The problem of the lesser circulation is very similar to that presented by a newborn infant: What is it going to develop into?"

This morning we have certainly seen what has developed in those seven years. Dr. Sante gave an excellent demonstration of the detailed anatomy of the lung. Miller's book had been out for several years, but it remained for Dr. Sante and the workers in that field to correlate those anatomical studies with the clinical findings.

Six years ago who of us would have expected to make a diagnosis of arsenical dermatitis, of lupus erythematosus, of trauma to the blood vessels of the lung, of periarteritis nodosa, or of acute rheumatic pneumonia from the roentgenogram? Dr. Barden in his excellent discussion brought this out to us and emphasized the important point that we must be familiar with the clinical findings in the patient whose films we are studying. In that way we sometimes can indicate to the clinician further studies to make the diagnosis.

Dr. Good gave a fine summary of the usual roentgenographic signs and problems of the lesser circulation. It was interesting to hear that the cause of death in hunchbacks is largely due to cardiac failure. I did not fully realize the tremendous significance that kyphosis and distortions of the thorax might play in influencing the cardiac symptoms.

Dr. Wasson has gone over the clinical problems of the lesser circulation. There is no need to repeat them here. In closing, Dr. Wasson, your infant of 1941 has grown into a Miss America, both in chronological age and as a national symbol, as most of the contributions in the diseases of the lesser circulation have been made by American physicians and American scientists.

Dr. David A. Cooper, Philadelphia, Pa. When a clinician goes to a radiologist, it is usually to gain knowledge—and that is pretty much my position here today. Among all the medical specialists, the radiologist is in the most unique position to observe living pathology and pathological physiology in the lung. I would like to congratulate your Program Committee as well as the various essayists who did beautiful jobs, but particularly the Committee that planned this anatomical, physiological and roentgenological approach to the study of a section of the body and its diseases where there is still something to be learned.

This group of papers has brought out the important manifestations in the lesser circulation of many and varied processes, and has again stressed the importance of considering man as a heart-lung preparation rather than one of independent organs, with diseases limited to each. From a clinical standpoint, our job is to recognize symptoms, and then with the aid, most often of the radiologist and the physiologist, to interpret them and correct them if possible.

The importance of pulmonary manifestations in heart disease or the cardiocirculatory manifestations of pulmonary disease have been stressed this morning; also the manifestations in the pulmonary circulation of various constitutional diseases. Time does not permit, nor does my knowledge justify, any attempted detailed discussion of these beautiful presentations. Taken together, they all give us a clearer picture and a better understanding of the effect in the lesser circulation of various disease states.

There is one thing in connection with Dr. Wasson's comments, and the only thing that has not been mentioned: his reference to the influence of respiration on the maintenance of circulation. It has recently been shown by Thompson, of New York, that after stopping

* Papers by Drs. Sante, Barden and Cooper, Dripps, Good and Dry, and Wasson.

the heart, circulation can be maintained by maintaining respiratory motion.

As an internist I want to thank you all for the privilege of being here and learning from the radiologist.

DR. JESSE E. EDWARDS, Rochester, Minn. As a pathologist, it is a great privilege for me to appear before this Society, and it is a distinct pleasure to take part in the discussion of this symposium, a symposium which obviously has been well planned and well executed.

I shall confine my remarks to the circulation of the bronchial arteries. The lesser circulation and the greater circulation are closely interrelated; and one of the important bridges between these two circulations is the system of bronchial arteries. I shall show several lantern slides, the first three of which were loaned to me by Dr. A. A. Liebow of the Yale University Medical School, Department of Pathology.

(Slide) The first three slides are injection preparations of the bronchial artery and pulmonary circulation, as well as of the bronchial system in human material. The bronchial arteries are in black, as is the aorta. The trachea and the bronchi, as well as the ramifications of the bronchi, are in white. The red portrays the location of the pulmonary arterial system; the green represents the pulmonary veins.

In this preparation, which is that of the normal bronchial circulation, small vessels—the bronchial arteries—arise either directly from the aorta or from the intercostal arteries. In the normal circulation, with the injection technique employed, the arteries are not seen in the pulmonary parenchyma. Dr. Liebow and his colleagues have shown that in the presence of bronchiectasis the bronchial arteries are increased in size.

(Slide) In this slide one can see that in bronchiectasis, anastomosis between the bronchial arteries and pulmonary arteries becomes visible. Here is a bronchus which is dilated, and we find here a bronchial artery; here is a branch of it, and here is a pulmonary artery. At this point the two systems visibly anastomose. There are actually numerous anastomoses in this area.

Recently, we have become interested in study of the lungs in cases of coarctation of the aorta, primarily for the purpose of determining whether or not the bronchial arterial system is altered in this condition. We know that the bronchial arteries arise from vessels which normally take part in the collateral circulation in the presence of coarctation of the aorta. Consequently, perhaps the bronchial arteries, as innocent bystanders, if nothing more, may carry a great volume of blood, and possibly this blood is under greater pressure than is normal.

(Slide) The next slide is a photomicrograph of a section of tissue from the lung in a case of coarctation of the aorta. Here is a cross section of a bronchus, showing the epithelium of that structure. In the lower part of the field is a portion of the bronchial cartilage. You will notice, around the epithelium, a vascular plexus, a collar of blood vessels, which probably represents an increase in the amount of blood flowing through those vessels which are supplied by the bronchial arteries.

Not only do we have evidence that the vessels which arise directly from the bronchial arteries carry a greater volume of blood, or blood that is under greater pressure, but there appears to be an increase in the amount of blood in the pulmonary arterial circulation.

(Slide) This is taken from the periphery of the lung, and we find very prominent wide, thin-walled pulmonary arterioles, so that we have here, by inference, if not more, at the present stage of the study, evidence that the pulmonary arteries in the presence of coarctation of the aorta do receive more blood than they do in the normal state.

Not only do the pulmonary arteries appear to be dilated and thin walled, which is evidence that they have been subjected to this stimulus for some time, but also, we find that there is pulmonary alveolar congestion.

(Slide) This slide is a photomicrograph, made with higher magnification, of a section of tissue from the lung, showing a dilated pulmonary arteriole. We see that the capillaries of the alveolar walls are filled and are tremendously distended.

It might be argued that this pulmonary congestion, which is marked, is the result of an acute cardiac failure, from which a number of patients with coarctation of the aorta die. On the other hand, the changes in the larger vessels are distinctly recognizable as anatomic changes, and they undoubtedly represent, as already stated, changes which have developed over a considerable period.

In addition to the congestion, we frequently find evidence of old hemorrhage into the alveolar spaces. It is not uncommon, in study of

sections of the lung in cases of coarctation of the aorta, to find many foci of alveolar spaces filled with hemosiderin-laden microphages, which are interpreted as being evidence of old alveolar hemorrhage.

(Slide) The next two slides represent sections of tissue taken from a patient who had the tetralogy of Fallot. The patient was a fourteen year old girl in whom the usual pulmonic systolic murmur was absent. The clinicians felt that there was complete atresia of the orifice of the pulmonary artery. Pathologically, the valve of the pulmonary artery was almost completely occluded; it admitted only the finest probe. To all intents and purposes, I think, the pulmonary artery was carrying virtually no blood to the lungs.

We have here a photograph of a posterior view of the thoracic organs in that case. Here is the left lung; here is the right lung; here is the esophagus; here is the trachea; over here is the aorta. From the second aortic intercostal artery on the right side we are able to pick up a large bronchial artery, which was easily cannulated and injected. It proceeded to the main bronchus of the right lung, and before that, it gave off a branch which crossed the esophagus and proceeded to the left lung. Undoubtedly, this bronchial artery was the main source of blood supply to the lungs of this patient who had the tetralogy of Fallot.

The observation that the bronchial arteries may carry a substantial amount of blood to the lungs in the presence of pulmonary stenosis is not original with us. In talking to Dr. Liebow the other day, I found that he has demonstrated the same thing recently, and there are reports of similar observations in the literature.

Dr. Felix G. Fleischner, Boston, Mass. I want to use my time as sparingly as possible. Roentgen kymography has been given a new impulse by the application of the photomultiplier tube, the use of which was first suggested in this country by Chamberlain. We in Boston, Dr. Luisada and I, have been using an arrangement similar to, but more sensitive than that devised by Chamberlain and co-workers. We have made observations on the lesser circulation which we thought might be of interest in connection with this morning's symposium.

(Slide) If the pick-up device with the photoelectric tube is placed across the pulsating border of the heart or a great vessel, it operates like a highly sensitive kymograph. While the classical roentgen kymograph registers directly the pulsating shadow on the film, in this new apparatus pulsating changes of light intensity, proportionate to pulsating movements, are being transformed into a pulsating electric current to be recorded by the galvanometer of a standard electrocardiograph.

Placed over the center of an opaque object, e.g. the hilar shadow, changes in the opacity of this object will be recorded by the apparatus. The same thing can be done by placing the pick-up device in any peripheral portion of the lung field.

(Slide) Just to familiarize you with the appearance of these tracings, I show you this slide. In order to time the various waves, we register simultaneously a phonocardiogram which shows the first and second sound. Here you see four different curves: From the left auricle, the left ventricle (at a high level), from the pulmonary artery, and the aorta. You can see the different shapes and amplitudes of these pulsations. They are all taken with the same amplification and sensitivity of the apparatus.

(Slide) You see here curves taken over the right hilum and the right lower lung field. I will not go into any analysis of the details of the curves, but perhaps you recognize that the peak of this curve, which represents the arrival of the pulse wave at the hilum, occurs about a tenth of a second earlier than that in the periphery of the lung field.

(Slide) For better comparison of the time relationship of several curves we can trace two pulsations simultaneously by a tribeam electrocardiograph. Here the lower curve represents the pulsation of the aortic arch, and the upper that of the pulmonary artery on the left side. You see a difference in the shape of the curves, the more pronounced dicrotic wave and an earlier arrival of the pulse in the pulmonary artery.

(Slide) Here I show you another tracing where we have in the lower curve a record of the right hilar vessels, and in the upper curve, with more magnification, the pulsation of the peripheral lung field.

It was most surprising, among our early observations, to see the pulsation of the periphery due to the small arteries of the pulmonary parenchyma, and this has never, to our knowledge, been seen before the application of this new principle. We believe that many interesting observations will be made in the future by this

method, both in the field of physiological research and in that of clinical application.

DR. SANTE (closing). I have only a word to say with reference to coarctation. It seems rather strange to me that coarctation of the aorta should cause such great enlargement of the bronchial arteries. Of course, the site of origin of the bronchial vessels from the aorta or from the intercostal or intramammary is so variable that perhaps the relationship of their origin might have something to do with it. It at least would certainly have something to do with whether or not the bronchial vessels came off above or below the site of coarctation.

It occurs to me that perhaps the explanation might be relatively simple in this regard. If you have a water pipe conveying water of a certain amount and divide it into two smaller divisions, one of which is larger than the other, depending upon the relative size of the two pipes, the amount of water that will go through the smaller will be less due to resistance. Perhaps the explanation is as simple as this. In other words, if you have an aorta of a certain size, which has been coarctated and reduced in caliber, and then a relatively normal sized bronchial artery, it seems obvious that the normal sized bronchial artery, competing with a coarctated aorta, may attain a greater size in proportion because it will get a greater amount of the fluid in proportion.

The fact that the vessels at the periphery of the lung were also dilated in the case that was shown also seems to bear out this reasoning and suggest it as a possible explanation.

VOL. 61, NO. 1

THE VALUE OF ANGIOCARDIOGRAPHY IN ESTABLISHING THE DIAGNOSIS OF PERICARDITIS WITH EFFUSION*

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THE diagnosis of pericarditis with effusion is often difficult. Even after the clinical history, physical examination, laboratory and roentgenological examinations it may be impossible to differentiate pericardial effusion from an enlarged or dilated heart. Angiocardiography has made it possible to visualize the cardiovascular structures and thereby differentiate dilated heart chambers and hypertrophied cardiac walls.[6,7,8] Our experience with 4 cases of pericarditis with effusion forms the basis of this report, and demonstrates how easily and without harm to the patient angiocardiography establishes the diagnosis.

The symptoms of pericarditis with effusion vary considerably from extreme dyspnea to mild pain. Often no symptoms are present until a tamponade effect is produced. The symptoms of cardiac enlargement also vary greatly and are inconstant. In addition, pericardial effusion may be found in the presence of rheumatic heart disease, hypertensive cardiovascular disease, coronary sclerosis, and in the terminal phase of cardiorenal failure. Pericardial effusion is also found in tuberculosis, pyogenic infections, and malignant disease.[1,10] The physical findings in pericarditis with effusion may be a pericardial friction rub, increase in the area of cardiac dullness, distant heart sounds, increased retromanubrial dullness, shift of cardiac dullness on change in position of the patient, and signs of compression of the left lung posteriorly. These signs are produced only in the typical case, are inconstant, and many of them are also present with cardiac dilatation and hypertrophy. The presence of pleural effusion, pulmonary parenchymal consolidation, or atelectasis further complicates the clinical picture and makes the diagnosis of pericarditis with effusion with or without associated cardiac enlargement difficult. Laboratory tests are usually of no direct help in distinguishing between pericardial effusion and cardiac enlargement. They may aid in establishing the presence of infection, heart or kidney disease, but pericardial effusion as a complication cannot be determined. Although the electrocardiogram shows some changes of diagnostic value, there are no specific findings that are characteristic of pericarditis with effusion.[1,12]

The appearance of the cardiac silhouette on roentgenologic examination is probably the most reliable sign of pericarditis with effusion. Roentgenoscopic examination will yield information regarding the pulsation of the cardiac shadow. In pericardial effusion, the pulsations are definitely diminished or absent, especially in the dependent portion of the cardiac silhouette. The usual active pulsation of the ventricular shadow is decreased or absent, and pulsation of the aortic shadow is relatively increased. However, a dilated or hypertrophied heart may produce similar findings. The change in shape of the cardiac shadow with change in position of the patient can be observed roentgenoscopically in a typical case of pericardial effusion. Roentgenographically, pericardial effusion is recognized by marked generalized enlargement of the cardiac silhouette with obliteration of the normal cardiac contours. In some cases a pear or water-bottle shaped shadow with a small aorta above it is formed. Enlargement of the cardiac silhouette most marked in its transverse diameter, with distention of the posterior inferior recess and foreshortening

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of the vascular shadow most evident with the patient in the recumbent position, and change in size and shape of the cardiac silhouette within a short interval of time can be recognized. These findings again are variable and marked cardiac enlargement will often present the same appearance.[2,9] It is well established that the heart cannot be seen as a separate shadow within the cardiac silhouette in pericarditis with effusion.[4,9] A chronic pericardial effusion may produce little or no effect on the lesser circulation, and no evidence of pulmonary congestion will be seen roentgenologically. However, pericardial effusion with cardiac enlargement is frequently associated with pulmonary vascular congestion. Roentgen kymography records the pulsations of the cardiac shadow and gives no more information than roentgenoscopy.



FIG. 1. Conventional roentgenogram. Female, aged fifty-six, admitted for treatment of active gastric ulcer. Known hypertension for three years. No cardiac complaints. Blood pressure 155/100, fair heart sounds. Left axis deviations in the electrocardiogram. Enlarged cardiac shadow with diminished pulsations roentgenographically. Note the generalized enlargement of cardiac silhouette with absence of pulmonary congestion.

Pericardial tap with removal of fluid is proof of the existence of pericardial effusion, but this procedure may be difficult, and, as Levine[5] points out, is hazardous. The injection of air into the pericardial sac after removal of fluid to visualize the effusion roentgenographically yields little additional information.

METHOD AND FINDINGS

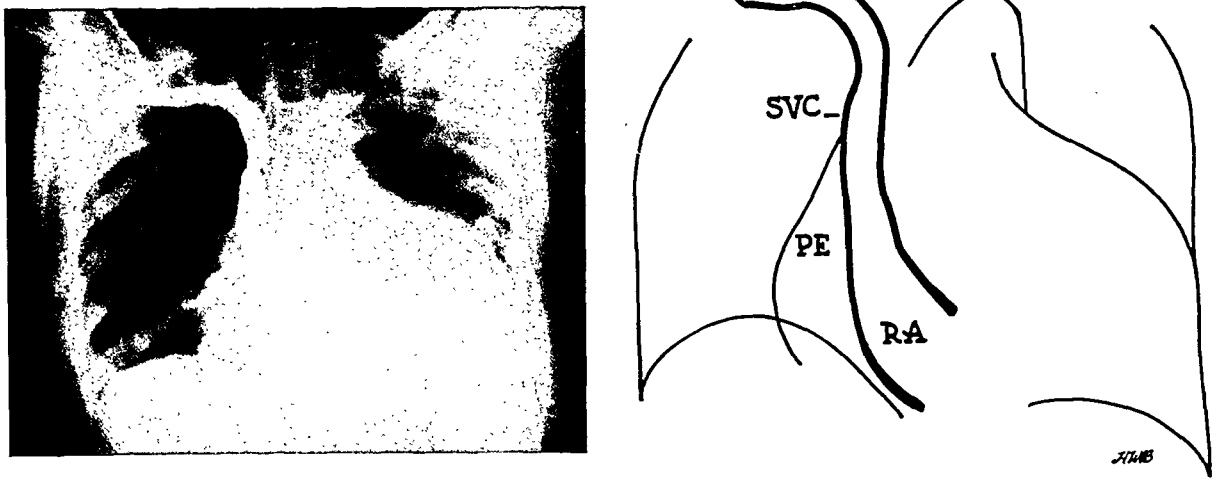
The Robb and Steinberg method of cardiovascular visualization[6,7] was used to study 4 patients in whom routine methods of investigation were inconclusive in establishing the diagnosis of pericarditis with effusion. Films were taken in the posteroanterior projection at appropriate time intervals to visualize the chambers of both sides of the heart. In each instance the opacified right and left cardiac chambers were seen to lie well within the cardiac silhouette, the intervening space representing the chamber walls and the fluid in the pericardial sac entirely surrounding the heart. Pericardial tap with removal of fluid confirmed the diagnosis in each case.

Figures 2 and 3 (Case I) illustrate the angiocardiographic appearance of a pericardial effusion. In this case its presence was not suspected clinically, but was clearly shown by angiocardiography. Case II was a patient who had hypertensive cardiovascular disease and chronic heart failure. He was not suspected of having a pericardial effusion clinically or by routine roentgenographic procedures because the enlarged cardiac silhouette was attributed to the hypertensive disease. Angiocardiographic studies demonstrated the presence of a pericardial effusion in addition to enlargment of the heart chambers. Cases III and IV were two patients in whom angiocardiographic studies revealed the presence of pericardial effusion. Both of these patients had pulmonary tuberculosis, and tuberculosis was believed to be the cause of the pericardial effusion. In one of these cases, repeat angiocardiography following subsidence of the pericardial effusion clearly demonstrated that the opacified cardiac chambers and their walls had resumed their normal border forming position. In all 4 of the patients in this study, no serious reactions were experienced either during or following angiocardiography. None of these patients had severe liver disorders, nephritis, hyperthyroidism,

or known allergic tendencies which are contraindications to the procedure.[6,7]

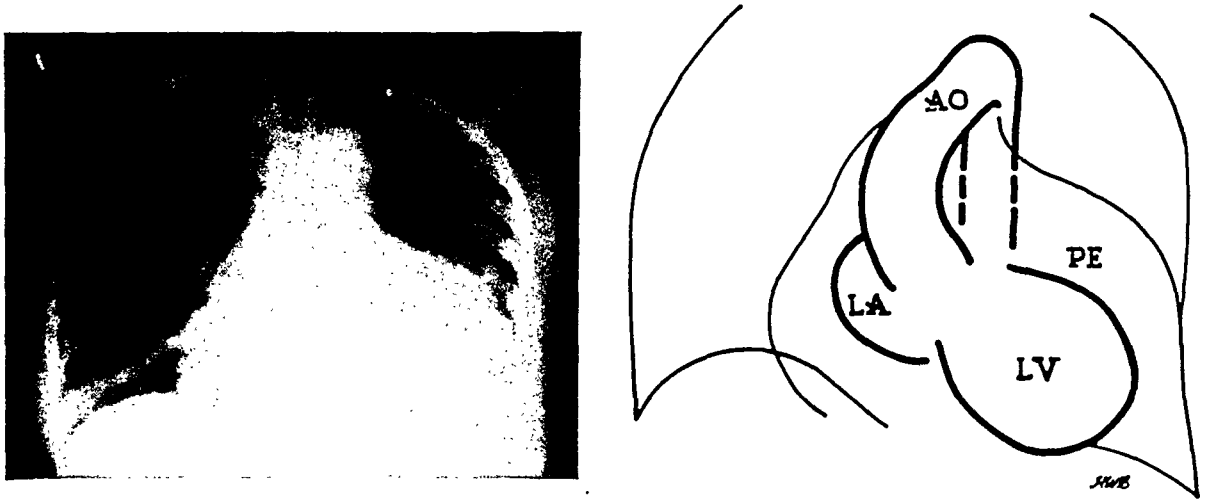
DISCUSSION

Shortly after cardiac visualization was described, it became apparent that this procedure could be used to establish the diagnosis of pericarditis with effusion, particularly in patients in whom clinical and laboratory findings were inconclusive.[6,7] Recently Ungerleider[11] made reference to this possibility. In our 4 cases the presence of pericardial effusion was demonstrated angiocardiographically by the visualization of the opacified cardiac chambers lying within the surrounding shadow of pericardial fluid. Because of the higher concentration of the opaque medium in the right side of the heart, the contrast between the opacified chambers and surrounding peri-



A B

FIG. 2. *A*, contrast roentgenogram at two seconds. Right subclavian, innominate, superior vena cava and right atrium visualized. Note the pericardial fluid shadow adjacent to right atrium. *B*, tracing of *A*. *SVC*, superior vena cava; *RA*, right atrium; *PE* pericardial effusion.



A B

FIG. 3. *A*, contrast roentgenogram at twelve seconds. Pulmonary veins, left atrium, left ventricle and aorta opacified. The shadow of pericardial fluid is seen beyond the left ventricle. *B*, tracing of *A*. *LA*, left atrium; *LV*, left ventricle; *AO*, aorta; *PE*, pericardial effusion.

cardial fluid was more striking than on the left. However, visualization of the left heart chambers in all cases likewise showed the pericardial fluid.

The posteroanterior view was used in these 4 cases, but the same information would be available if patients were studied in other projections. In each instance the patient had no ill effects from the injection of contrast medium. In one case the study was repeated to show the disappearance of the pericardial fluid.

The differentiation between pericardial effusion and cardiac enlargement due to dilated chambers or hypertrophied walls was easily made angiocardiographically. The appearance of cardiac chamber enlargement and thickened cardiac walls has been described in previous reports.[3,8] While the shadow beyond the opacified chambers in pericardial effusion represented both the thickness of the cardiac wall and the pericardial fluid, the diameter of the shadow was well beyond the limits of hypertrophied cardiac walls. Patients with mediastinal masses adjacent to the pericardium were clearly differentiated from pericarditis with effusion by showing the unilateral character of the masses, whereas, in pericardial effusion, both the right and left sides of the heart were surrounded by shadow of the fluid in the pericardial sac. A pericardial cyst has not been encountered, but it is believed that its unilateral location should differentiate it from pericardial effusion.

CONCLUSIONS

(1) Angiocardiography of four patients with pericarditis with effusion demonstrated a characteristic shadow due to the fluid surrounding the opacified cardiac chambers.

(2) The fluid density could be easily differentiated from normal or hypertrophied cardiac walls.

(3) Angiocardiography will establish the diagnosis of pericardial fluid in those cases in which the routine clinical and laboratory findings are inconclusive.

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ADDENDUM

Since this paper was submitted for publication, we have demonstrated the presence of pericardial effusion by angiocardiography in 5 additional patients in whom clinical and roentgenologic findings were inconclusive.

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A RAPID METHOD OF ROENTGENOLOGIC EXAMINATION OF THE SMALL INTESTINE*

A PRELIMINARY REPORT

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AT THE present time there is no standardized technique for the roentgenologic examination of the small intestine, and each roentgenologist has more or less his own method of procedure. Hodges, Rundles and Hanelin[2] for instance, advise one, two and a half, and five hour abdominal films for the initial examination of the small intestine with a second more detailed study when indicated. Schatzki[4] recommends the small intestinal enema first described by Pesquera[3] in 1929. Although this method is rapid, and good visualization of the small intestine is obtained, it necessitates the passage of a duodenal tube, and is practical only in selected cases. Golden[1] examines the entire small intestine by means of roentgenograms taken at half hour intervals supplemented by roentgenoscopy and spot films as indicated. Even though the incidence of small intestinal disease is low, every examination of the small intestine should be thorough and not a casual observation by means of one or two abdominal roentgenograms taken at irregular intervals. The principal disdvantage of any thorough examination is that it requires time-consuming efforts on the part of the patient, the roentgenologist, the technician, and the roentgen department. This is an important consideration when large groups of patients are examined. With all present routine methods of small intestinal examination, the time involved is from three to six hours and frequently longer. With a rapid method of examination, this time factor, and the expense element as well, would be decreased, and there would be more incentive for more frequent investigations of the small intestine.

METHOD AND RESULTS

In 1941, one of us (S. W.) noted the effect produced by an iced drink after a full meal, namely, a marked increase in the motility of the contents of the gastrointestinal tract with resultant diarrhea. Some investigations along this line were conducted by him at that time, which showed roentgenographically that ice water, given after a barium-water meal, produced a marked acceleration of the movement of the meal through the small intestine. We verified these findings in a number of normal cases and found that in about 50 per cent the head of the barium-water meal reached the cecum in one-half hour or less. This procedure was unsatisfactory because there was incomplete filling of the small intestine and distortion of the mucosal pattern. We then conducted small intestinal studies on 90 normal cases using a cold weak solution of sodium bicarbonate. With this method the motility of the gastrointestinal tract was increased above that obtained with cold water alone, but again the mucosal pattern of the small intestine was unsatisfactory. We then decided to use a barium-normal saline meal rather than a barium-water meal. One of the functions of the small intestine is to make hypertonic or hypotonic solutions isotonic. It would be expected that with a barium-isotonic normal saline meal the small intestine would have less work to do, and consequently the transit time would be decreased, and the mucosal pattern would be more normal. Golden[1] employs a barium-saline mixture in gastrointestinal examinations because of its more physiologic action. Accordingly, we determined the comparative motility of a barium-saline meal

* Presented before the New York Roentgen Society, New York, on January 19, 1948, and before the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14-17, 1948.

TABLE I

PROGRESSION OF BARIUM-WATER MEAL THROUGH SMALL INTESTINE IN ONE HOUR IN 107 NORMAL CASES

Position of Head of Meal	Number of Cases	Per Cent of Cases
Jejunum	32	30
Proximal ileum	19	18
Distal ileum	32	30
Cecum and beyond	24	22

TABLE II

PROGRESSION OF BARIUM-SALINE MEAL THROUGH SMALL INTESTINE IN ONE HOUR IN 114 NORMAL CASES

Position of Head of Meal	Number of Cases	Per Cent of Cases
Jejunum	8	7
Proximal ileum	21	18
Distal ileum	24	21
Cecum and beyond	61	54

and a barium-water meal. First, using a barium-water meal, routine one hour roentgenograms were taken as part of upper gastrointestinal tract examinations. The results are shown in Table I. Note that in 22 per cent of 107 normal cases, the head of the barium-water meal has reached the cecum in one hour. Next, using a barium-normal saline meal, one hour abdominal roentgenograms revealed results as shown in Table II. Note that in 54 per cent of 114 normal cases the head of the barium-normal saline meal has reached the cecum in one hour.

It is apparent, then, that a barium-saline mixture passes through the small intestine more rapidly than does a barium-water mixture. The barium-saline meal also produces less distortion of the mucosal pattern, and more adequate filling of the small intestine.

To utilize the accelerating effect of both saline and of a cold liquid, we devised the following technique of small intestinal examination and present it as a practical and accurate method.

TECHNIQUE OF RAPID METHOD OF SMALL INTESTINAL EXAMINATION

1. Roentgenoscopic and roentgenographic examination of the esophagus, stomach and duodenum (using 4 oz. barium and 4 oz. isotonic normal saline at room temperature).
2. Patient drinks 8 oz. of ice cold normal saline.
3. 14 by 17 inch abdominal film taken at five minutes.*
4. Patient drinks a second 8 oz. of ice cold normal saline immediately after the five minute film.
5. 14 by 17 inch abdominal film taken at fifteen minutes.*
6. 14 by 17 inch abdominal film taken at thirty minutes.*
7. All three abdominal films are shown "wet" to the roentgenologist who roentgenoscopes and takes spot films of suspicious areas, or if the head of the meal has reached the cecum, may roentgenoscope and spot the terminal ileum.
8. If the head of the meal has not reached the cecum, additional films are taken at half hour intervals until it has. The roentgenologist then roentgenoscopes and takes spot films as indicated.

The results of this method in 87 normal and 17 pathological cases are shown in Table III. Note that of 87 normal cases, in

TABLE III

RESULTS OF RAPID METHOD OF SMALL INTESTINAL EXAMINATION IN 87 NORMAL AND 17 PATHOLOGICAL CASES

Head of Barium-Saline Meal in Cecum or Beyond	Normal	Pathological†
½ hour or less	72 (83%)	8
½ to 1 hour	6 (7%)	2
More than 1 hour	9 (10%)	7

† Pathological cases:
2—chronic duodenal ulcer
2—sprue
2—sarcoma second duodenum
5—"deficiency" states
3—active duodenal ulcer
3—regional ileitis
1—ulcerative colitis

* Note that all times are taken from the time of drinking of the first 8 oz. of the ice cold normal saline.

72 (83 per cent) the head of the barium-saline meal had reached the cecum in one-half hour or less. In an additional 6 cases (7 per cent) the meal had reached the cecum in one-half to one hour. Thus, out of 87 normal cases, the head of the barium meal reached the cecum in one hour or less in 78 (90 per cent). In only 9 (10 per cent) did it take more than one hour for the head of the meal to reach the cecum. The mucosal pattern, in all cases, was as good as that obtained on routine small intestinal examinations and in several cases, much better, especially in the terminal ileum where there was a more even distribution of barium. In 42, or about 50 per cent, of the total number of normal cases the barium had entered the cecum in five to fifteen minutes. In several instances the head of the meal had reached the descending colon or rectum at fifteen minutes. In 10 out of 17 pathological cases the head of the meal reached the cecum in one hour or less. Most "deficiency patterns" or more properly called "disordered motor function patterns" were associated with a delay in passage of the barium meal through the small intestine, and all cases of regional enteritis showed no appreciable delay.

REPORT OF CASES

Case 1. Male, aged fifty. No clinical evidence of organic disease in gastrointestinal tract. This was a routine work-up. Small-intestinal study with the rapid method shows no evidence of disease and the head of the meal has reached the cecum in thirty minutes (Fig. 1, *A*, *B*, C).

Case 11. Male, aged forty-three, with known duodenal ulcer for twenty years admitted because of abdominal pain, tarry stools, and clinical evidence of vitamin deficiency. Gastrointestinal series with rapid small bowel examination shows a deformed duodenal bulb with a niche. A "deficiency pattern" is demonstrated with the head of the meal in the cecum in sixty minutes (Fig. 2, *A*, *B*, *C*, *D*). The deficiency state was believed due to inadequate diet in the presence of long standing duodenal ulcer.

Case 111. Male, aged fifty-seven, admitted because of weakness and copious, foul-smelling stools. Gastrointestinal series with rapid small bowel study shows abnormal small bowel pattern characterized by coarsening of mucosal folds, segmentation and dilatation with delay in transit time (Fig. 3, *A*, *B*, *C*, *D*). Laboratory studies established the diagnosis of non-tropical sprue (total fat in stool—37.6 per cent of dry weight). Patient was treated with vitamins, high caloric, low fat diet, liver extract, and folic acid with marked clinical improvement.

Case 1v. Male, aged thirty-six, with anemia for two years for which he had a splenectomy at another hospital. No history of any gastrointestinal symptoms. Gastrointestinal series with rapid small intestinal study reveals constant filling defect in the proximal jejunum, interpreted as carcinoma (Fig. 4, *A*, *B*, *C*). Laparotomy was performed and an adenocarcinoma of the proximal jejunum was found.

Case v. Male, aged twenty-five, first admitted in 1946 because of diarrhea of three years' duration. Gastrointestinal series with small intestinal study by means of hourly films showed terminal enteritis. Under medical treatment he gained weight and diarrhea decreased. Gastrointestinal series using barium-water meal with small intestinal study by means of hourly films was done on June 2, 1947, and showed no appreciable change. Figure 5, *A*, *B* and *C* show the appearance of the small intestine at four, five and six hours. During the next six months, be showed no change clinically and received no additional treatment. Gastrointestinal series with rapid small intestinal study was done on January 5, 1948 (Fig. 5, *D*, *E*, *F*). The lesion is well demonstrated and spot roentgenogram (Fig. 5, *G*) shows the extensive involvement with polypoid changes in the mucosa of the terminal ileum.

DISCUSSION

By using a barium-normal saline mixture as the contrast medium followed by ice cold normal saline, we were able to obtain a marked decrease in the transit time of the meal through the small intestine without distorting the mucosal pattern. In many cases the mucosal pattern was more clearly delineated, and there was more complete filling of the entire small intestine than

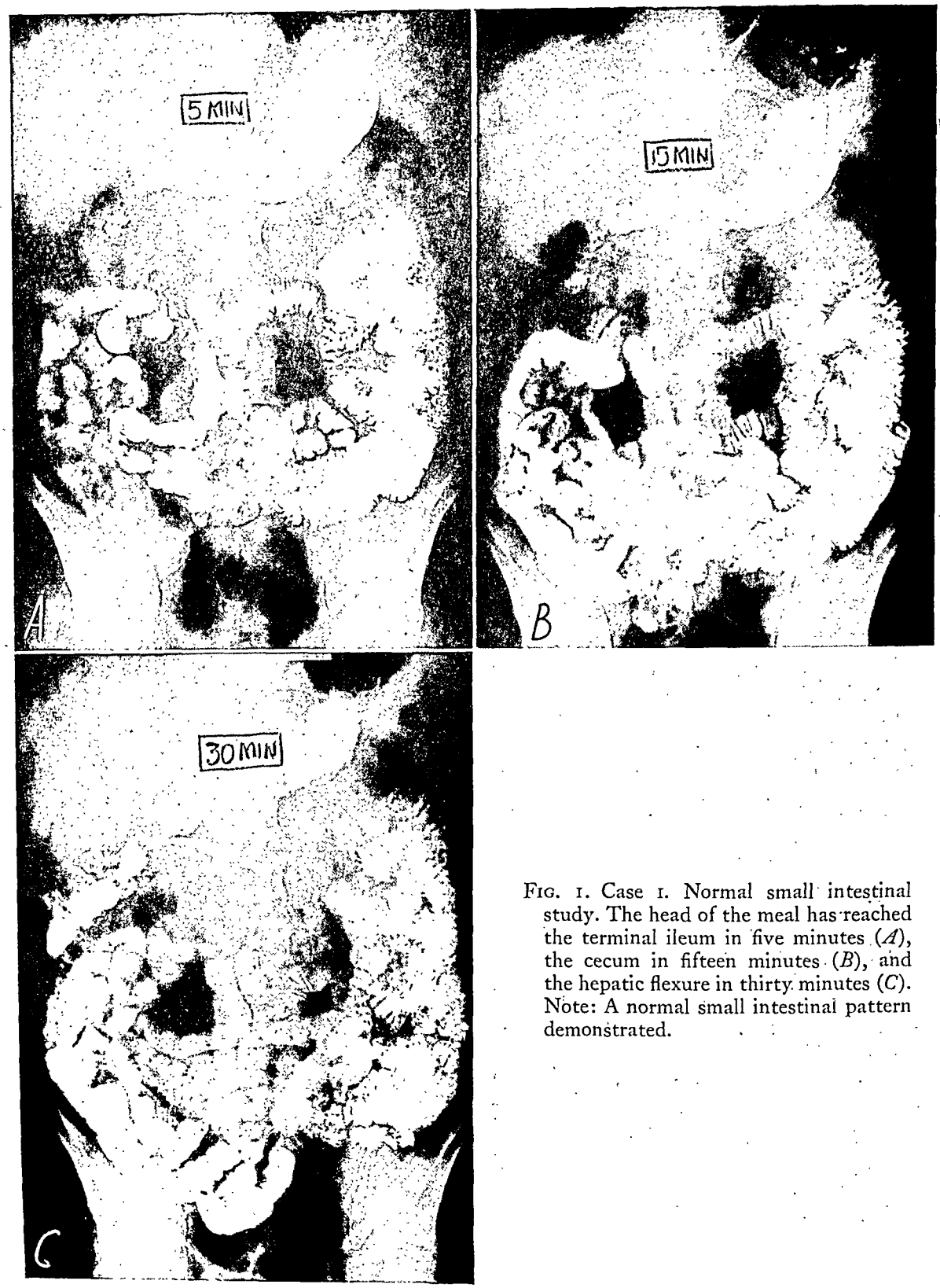


FIG. 1. Case 1. Normal small intestinal study. The head of the meal has reached the terminal ileum in five minutes (*A*), the cecum in fifteen minutes (*B*), and the hepatic flexure in thirty minutes (*C*). Note: A normal small intestinal pattern demonstrated.

that obtained by the hourly film technique. In 90 per cent of the normal cases studied, the examination was completed in one hour. In pathological cases, the rate of transit was also accelerated without sacrificing the appearance of the lesions.

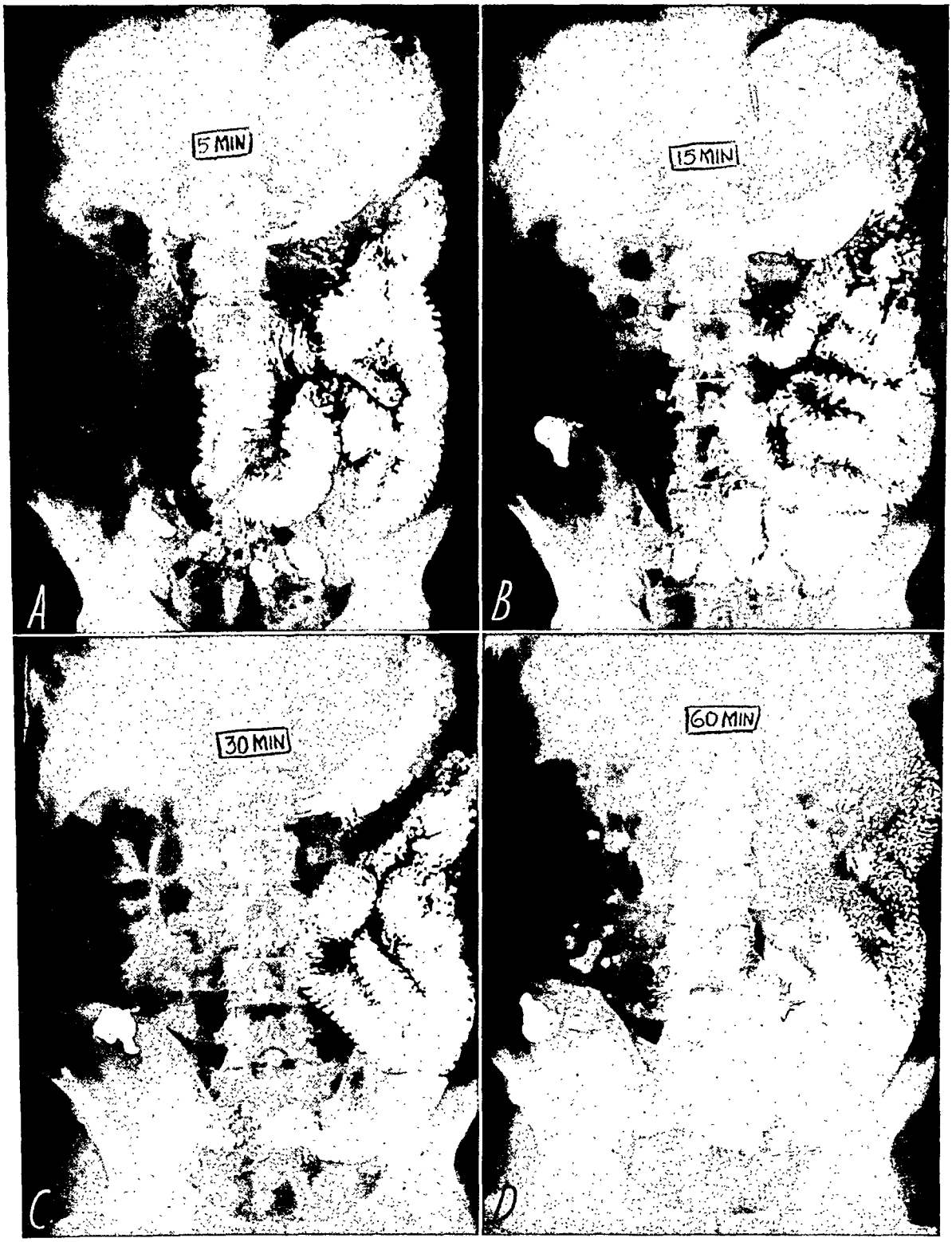


FIG. 2. Case II. Chronic duodenal ulcer with activity and "deficiency state." The head of the meal is in the distal jejunum in five minutes (*A*), with little further progression of the meal in fifteen minutes (*B*) and thirty minutes (*C*). The head of the barium meal has reached the cecum in sixty minutes (*D*). Note: The delay in transit of the meal by standards of this method. The deficiency state is recognized by the abnormal pattern; coarsening of the mucosal folds, segmentation, dilatation and flocculation.

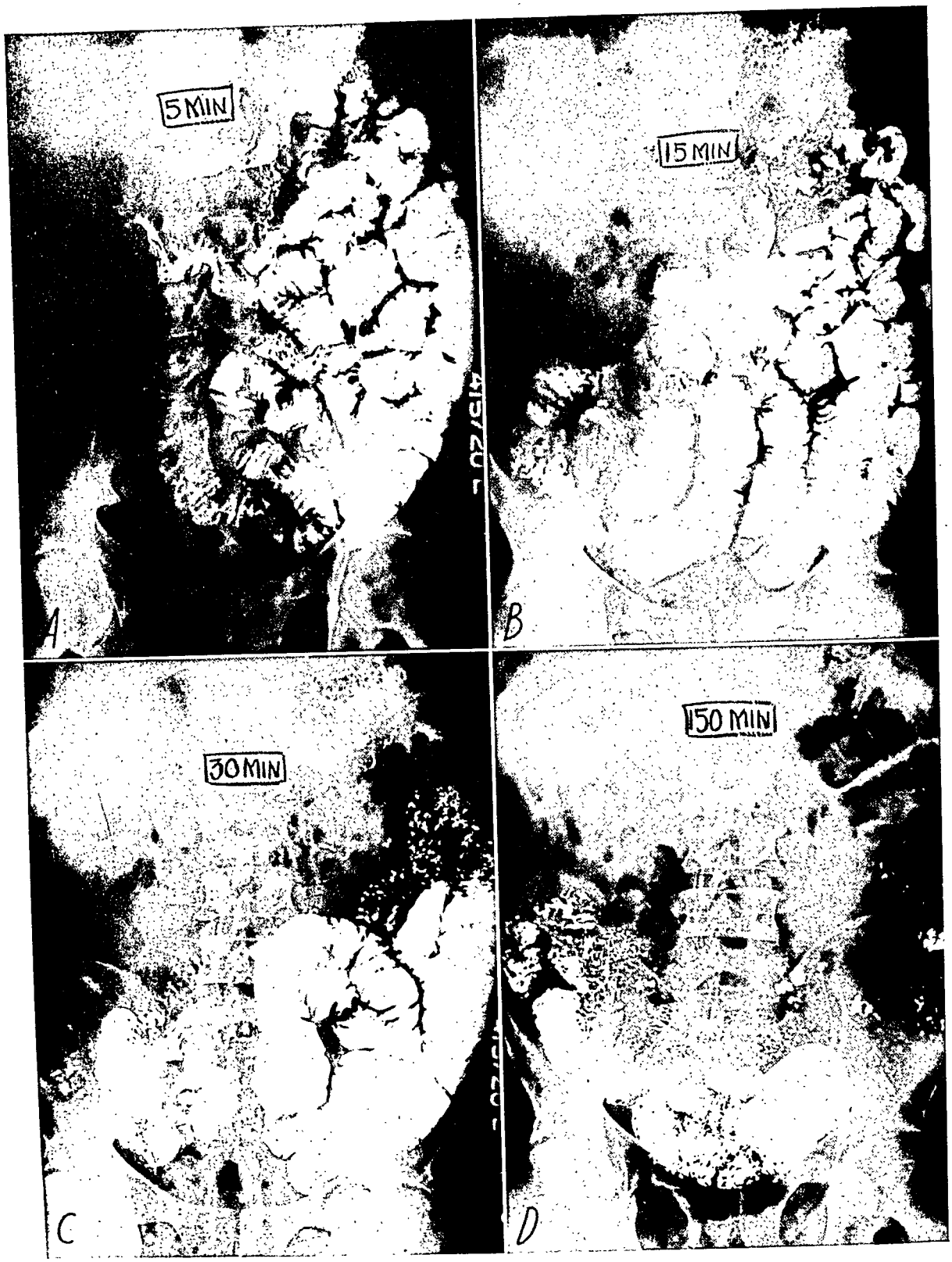


FIG. 3. Case III. Non-tropical sprue. The head of the meal is in the distal jejunum in five minutes (*A*), in the proximal ileum in fifteen minutes (*B*), and is still in the ileum at thirty minutes (*C*). The head of the meal has finally entered the cecum at 150 minutes (*D*). Note: The delay in transit of the meal by standards of this method, abnormal small intestinal pattern characterized by extensive dilatation, segmentation and flocculation most marked in the jejunum and proximal ileum.

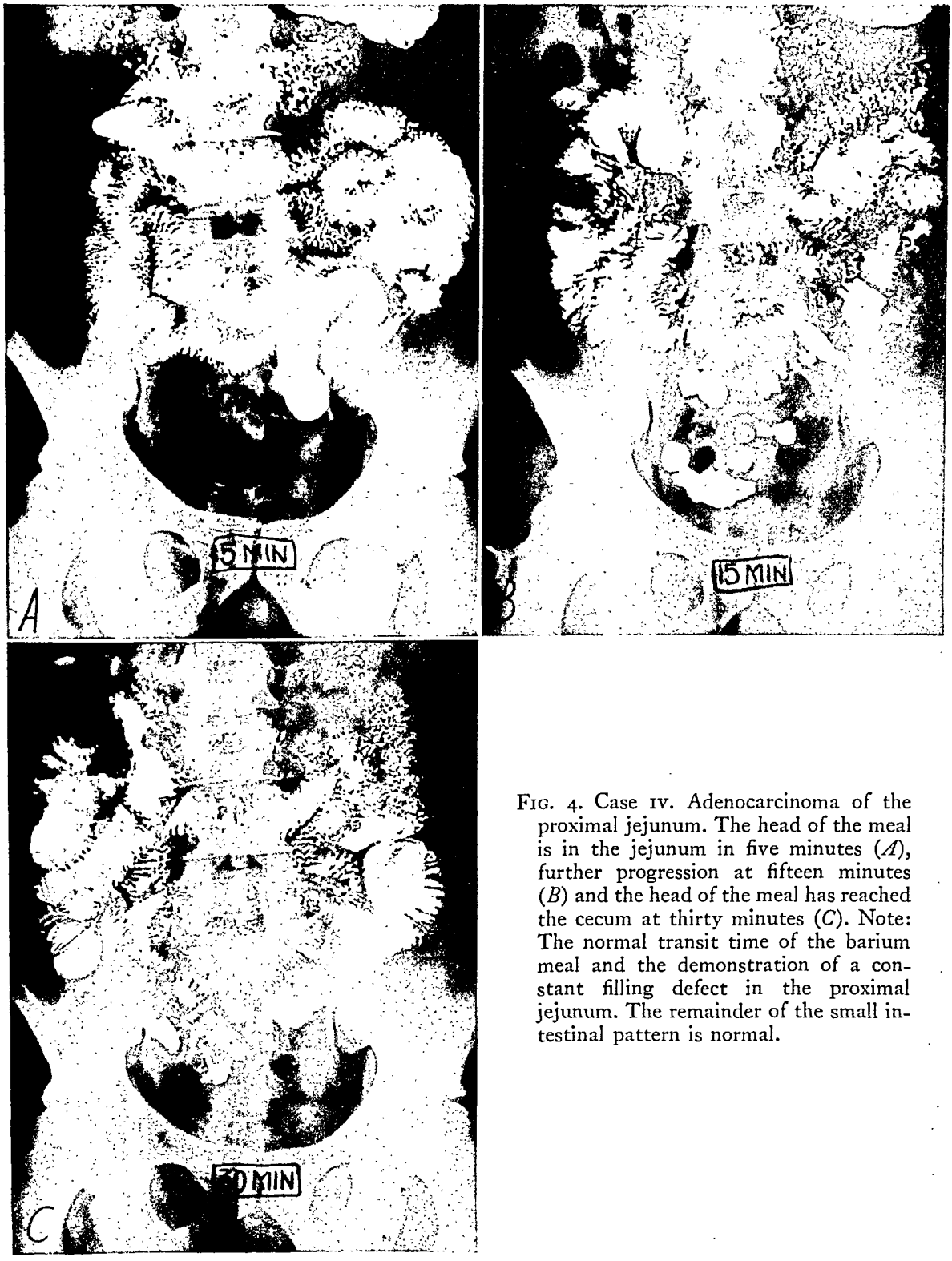


Fig. 4. Case IV. Adenocarcinoma of the proximal jejunum. The head of the meal is in the jejunum in five minutes (*A*), further progression at fifteen minutes (*B*) and the head of the meal has reached the cecum at thirty minutes (*C*). Note: The normal transit time of the barium meal and the demonstration of a constant filling defect in the proximal jejunum. The remainder of the small intestinal pattern is normal.

It is well known that in "deficiency states" or "disordered motor function patterns" and in sprue, there is a marked delay in the passage of the barium through the small intestine. We found this to be true with our method of examination, but the delay is only relative. For instance in one case of sprue (Case III), the head of the meal reached the cecum in 150 minutes. With the hourly method of examination it would

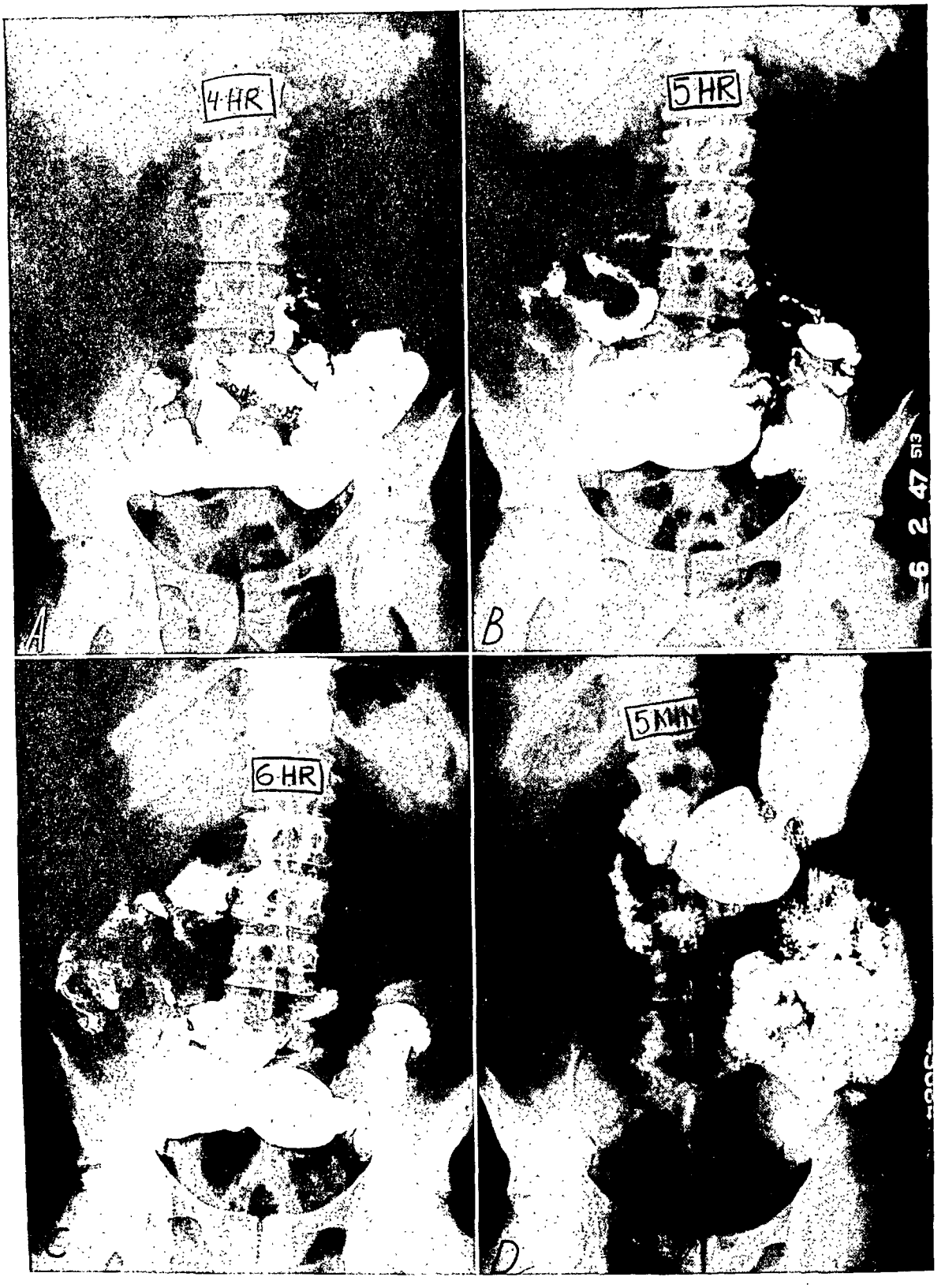
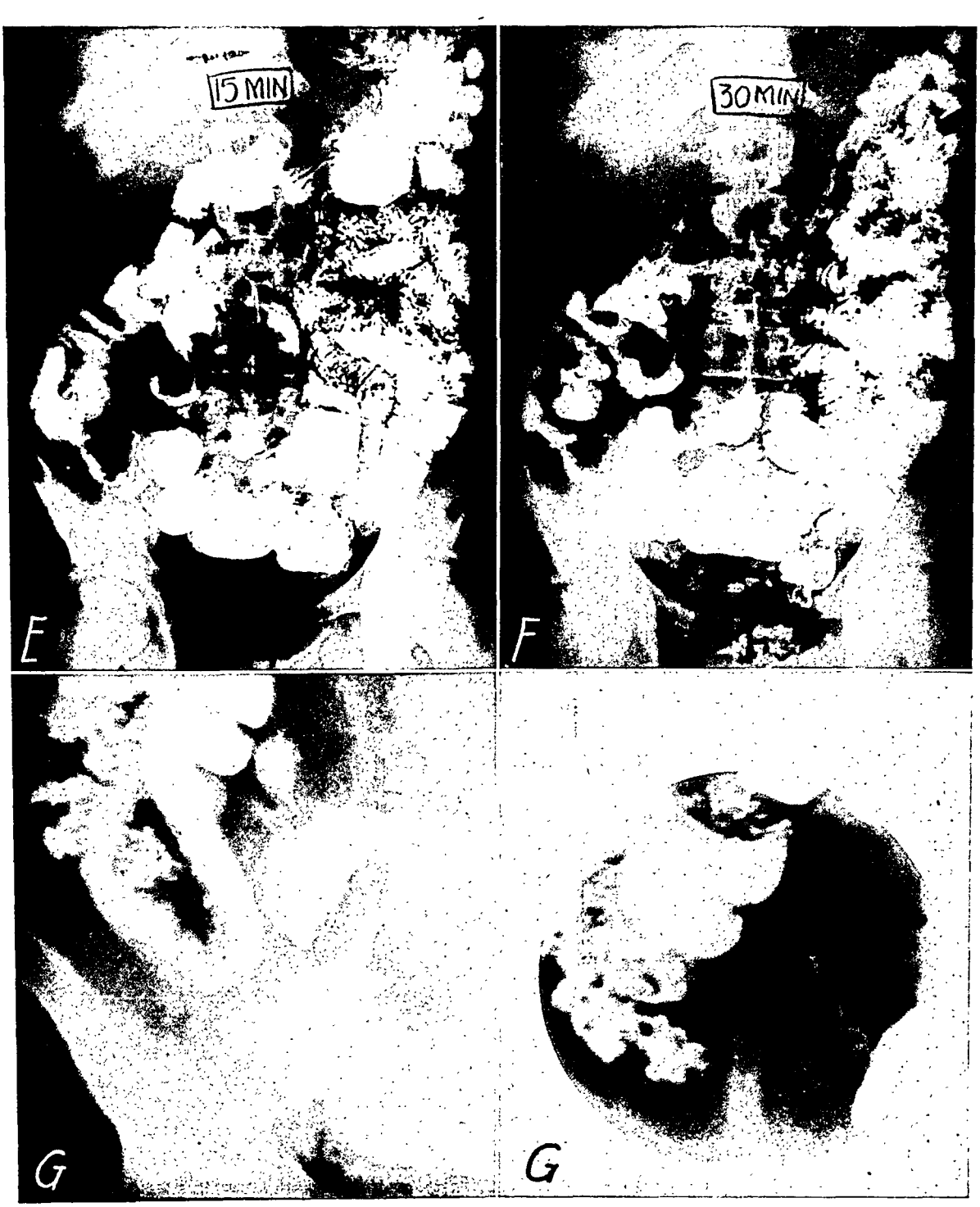


FIG. 5. Case v. Regional enteritis. (*A*), (*B*) and (*C*), four, five and six hour roentgenograms of examination of June 2, 1947. The head of the meal is in the transverse colon at six hours. (*D*), (*E*), (*F*) and (*G*), five, fifteen and thirty-minute roentgenograms of examination of January 5, 1948, and spot roentgenograms of terminal ileum. The head of the meal has reached the descending colon at fifteen minutes and the rectum at



thirty minutes. Note: There is better demonstration of the pathological areas with the rapid method than with the hourly film method. The "string sign," and abnormal dilatation of the ileum are well shown on the fifteen and thirty minute films and on the spot films taken during fluoroscopy at thirty minutes. The fifteen minute films show further advance of the barium meal than does the six hour film.

have taken six to eight hours. Tumors of the small intestine can be well demonstrated with the rapid method (Case IV). In our cases of regional enteritis the lesions are better shown with the rapid method, and no delay in transit time is noted. In Case V, for example, the fifteen minute film of the rapid method is superior to the

six hour film of the hourly method.

The physiological basis of this rapid method has not been fully investigated as yet, but we feel that there are three main factors to be considered: (1) the accelerating effect of the increased mass of solution (total of 24 oz.) and the dilution of the barium meal; (2) the stimulation of peristalsis by a cold solution, and (3) the more physiologic action of a normal saline solution as compared to that of a water solution. With the more dilute barium mixture there is less dehydration and consequently less clumping of the barium and better filling of the small intestine, particularly of the terminal ileum.

SUMMARY

1. A rapid and practical method of roentgenologic examination of the small intestine has been presented.

2. In 90 per cent of the 87 normal cases studied with this method, the barium meal reached the cecum in one hour or less. The entire small intestine was delineated satisfactorily, and the normal mucosal pattern was not disturbed.

3. In 17 cases in which lesions were present, they were demonstrated equally as well with this method, and in some cases better than with the hourly technique.

ADDENDUM

Since submission of this paper further clinical studies with the rapid method showed that in 91 per cent of 235 normal cases the head of the meal reached the cecum in one hour or less. In 46 abnormal small intestinal cases the lesions were as well demonstrated with this method and in several instances were shown to better advantage than with the hourly film method Physiologic studies showed that the principal factor in this method is the action of a cold solution in relaxing gastric tonus and opening the pylorus. This accelerating action of a cold solution has been evaluated by Gershon-Cohen, Shay and Fels.[5]

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DISCUSSION

Dr. Ross Golden, New York. Drs. Weintraub and Williams have presented a new method for the examination of the small intestine. They remark that there is no standard technique for the study of the small intestine. Many years ago, Pendergrass suggested 5 oz. of barium in distilled water as a standard barium meal. For him, this was a standard technique. We used it for a number of years, and then decided to try normal saline as a more logical medium from the physiological point of view, and through experience this has become standard for us. Dr. Pendergrass tried using normal saline and did not like it because he thought it made the transit time too short. What we like sometimes depends upon what we are used to. To me, it seems more important for each of us to use a technique the results of which we understand than for all of us to use exactly the same technique.

Drs. Weintraub and Williams compared their "rapid method" using cold saline to the distilled water medium at room temperature. It is not surprising that barium with cold saline goes through the intestine faster than barium with distilled water at room temperature because a saline preparation at room temperature goes through faster than barium in distilled water. Using this saline suspension at room temperature the barium reaches the cecum in one to one and a half hours in many cases. Inasmuch as Drs. Weintraub and Williams have their standards well set up for the cold saline method it would be interesting for them to compare it with the saline method at room

temperature. However, when barium enters the cecum, the examination is not necessarily over. The cecum is not always well filled at first and its appearance temporarily may not be normal. Furthermore, it is important to determine whether an apparent defect in any portion of the small intestine persists. Evidence of a disorder of the motor function of the intestine may be delayed. Furthermore, it is important to observe the effect of food on the intestine. After barium enters the cecum, we give a glass of milk. This is not only a food, but it is also one of the commonest of allergens. In a number of instances an overactive response has led to a suggestion that milk allergy might play a role in the clinical problem. If these points are borne in mind, I see no objection to the use of a large quantity of ice cold saline to hurry the barium along. We have used this Weintraub and Williams technique in a few cases and believe that it will probably prove in the long run to be a time saver. In cases of disordered motor function due to hypoproteinemia and edema, a tumor mass may not be outlined unless the barium is forced along rapidly and gives a continuous filling in spite of segmentation. This method may replace the small intestinal enema for this purpose.

THE PROCUREMENT AND CRITICAL APPRAISAL OF THE WIDTH DIAMETER OF THE MIDLINE RETROGASTRIC SOFT TISSUES

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THE main purpose of this paper is to describe and to illustrate how the simple barium opacified stomach can be utilized to obtain the midline width of the retrogastric soft tissues if used in conjunction with the proper roentgen projections, posture and position.

In 1934 Engel and Lysholm described gastric pneumography. They filled the stomach with air or gas and took translateral films with the patient in the prone position. The air by rising would approximate the posterior wall of the stomach to the retrogastric soft tissues. Since that time the method has been used to a limited extent, either utilizing a small caliber stomach tube or effervescent powders. The stomach tube method, while unpleasant from the patient's standpoint, had the advantage of permitting withdrawal of residual stomach fluid. It also controlled the amount of air administered and permitted decompression if the patient became uncomfortable. Nevertheless, unintentional overdistention has been the cause of perforation of some existing ulcers. Often it was found that the air or gas failed to distinctly outline the posterior stomach wall and that the routine study with barium sulphate was interfered with.

Engel and Lysholm stated that the retrogastric soft tissues are equivalent in thickness to the anteroposterior diameter of the lumbar body at any level measured and that any increase in this thickness would be pathologic. Critical appraisal, however, even after applying proper correction for habitus, posture, height, weight, age, sex, respiratory state, stomach filling state and other possible variables, has convinced us that such is not true, because the posterior wall of the stomach varies considerably as regards its relationships. The cardia, and in some, a considerable portion of the body or even the entire pylorus, may be to the left of the midline lying in the left parasagittal region in the plane of the lower posterior ribs and musculature of the left lateral gutter. In such cases, in order to obtain the retrogastric soft tissue thickness, one would need a measurement to the posterior abdominal wall along the recessed gutter and not to the midline lumbar bodies.

We have abandoned the use of air and have substituted barium sulphate. This has necessitated that the patient's position be reversed from prone to the supine in order to bring the posterior wall of the stomach as close as possible to the spine, utilizing the weight of the barium in the stomach. Thus the passage of a stomach tube is obviated and the procurement of the routine films is not interfered with. Accordingly, our method consists of the administration of an ordinary barium sulphate mixture and the taking of translateral (left to right) and anteroposterior views. It is very important to fill the stomach completely and to obtain the exposures immediately, especially the translateral, in order to avoid gravitation of the barium into the cardia.

First, the translateral view is taken. Next without moving the patient and immediately after, in the same respiratory phase, the anteroposterior view is obtained. Thus a correlated biplane study is accomplished and errors due to change in position, posture, respiration and the state of stomach filling are avoided.

It is obvious that if any measurement is to be valid it must be taken from the posterior wall of only that portion of the stomach that crosses the midline to the anterior vertebral margin at the level of

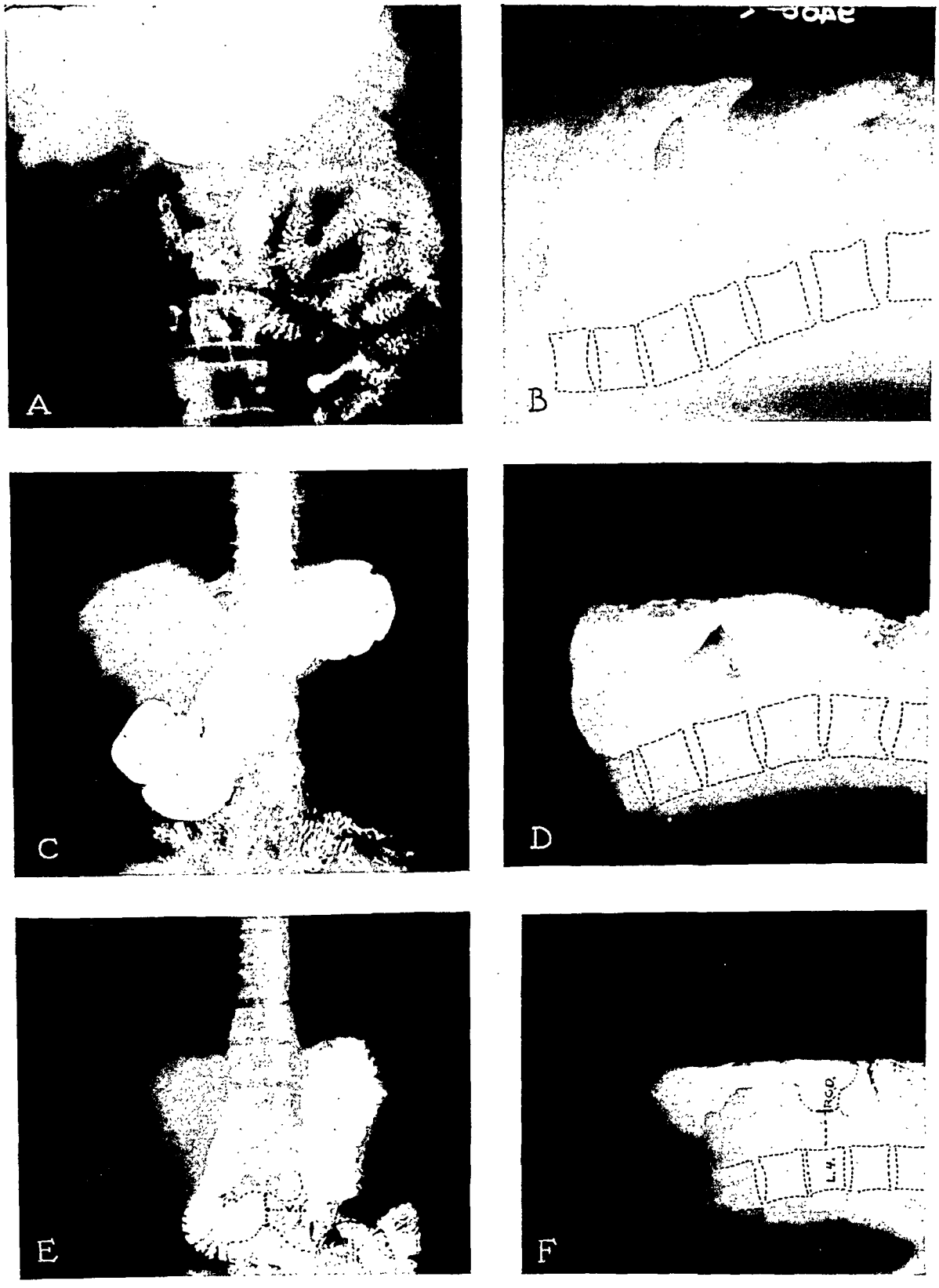


FIG. 1.* The various normal forms of habitus are illustrated in the anteroposterior and supine translateral projections: *A* and *B*, hypersthenic; *C* and *D*, sthenic; *E* and *F*, hyposthenic. These two films also illustrate how to obtain the vertical indicator (*V.I.*) by measuring the mid-distance between the lesser and greater curvatures of that portion of the stomach crossing the midline in the anteroposterior view. It is seen to be at the mid-level of the fourth lumbar body. This is then transposed to the exact vertebral level on the translateral and a perpendicular line from the anterior surface of the body to the nearest portion of the stomach is drawn. This is the retrogastric diameter (*R.G.D.*) in the midline.

* The illustrations were prepared by Mr. Sidney Shapiro.

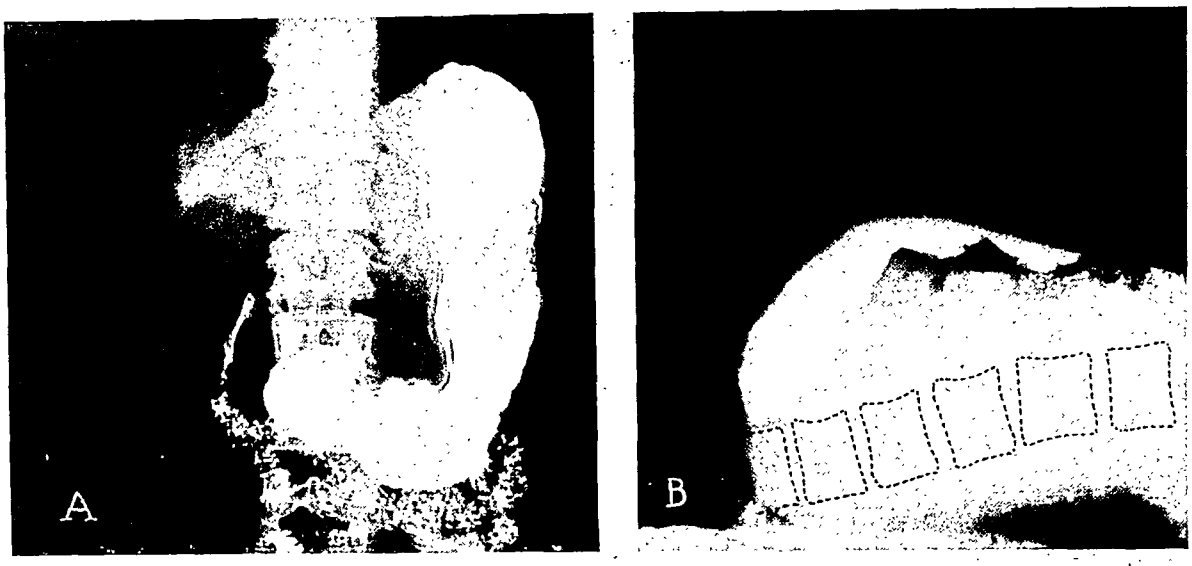


FIG. 2. This case illustrates the erroneous concept of measuring any other distance but the midline diameter. Ordinarily, this case would be considered abnormal, but measurement of the midline retrogastric diameter will show it to be normal.

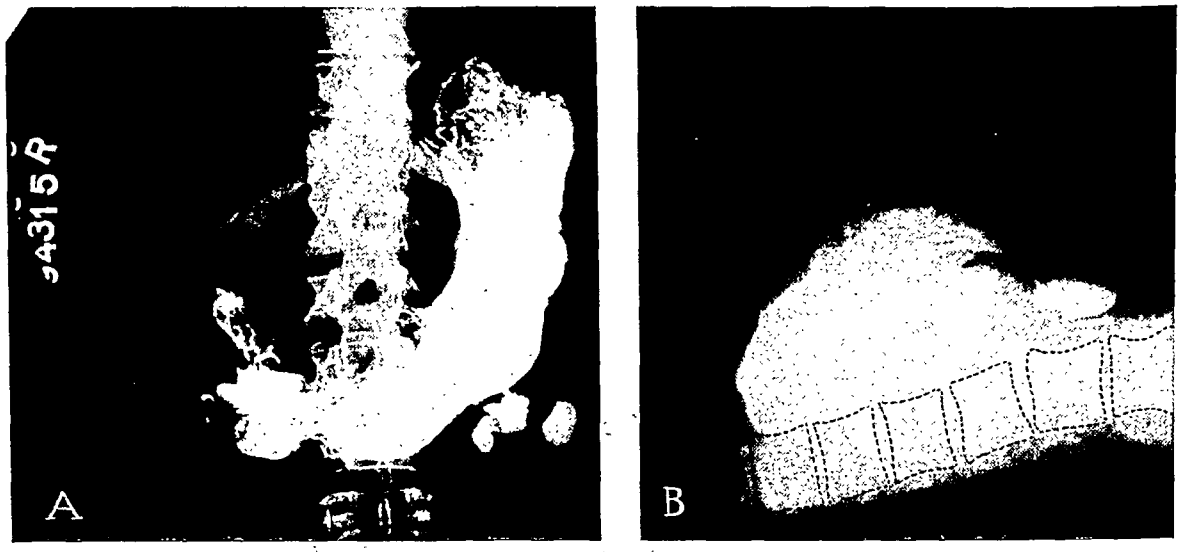


FIG. 3. This case shows an increase in the retrogastric midline soft tissue diameter due to cancer of the pancreatic head. Note the fistula from the prepyloric region to the pancreas.

crossing, otherwise the measurement would be an oblique one and it would be measuring the distance from a midline structure (vertebral body) to a portion of the stomach away from its anterior surface and therefore not related to it.

The anteroposterior view is the orientation film and is specifically taken to determine the exact vertebral body level at which any protion of the stomach crosses the midline. This is resolved to a point by mid-distance between the lesser and greater measuring the curvatures of that portion of the stomach crossing the midline. This point is called the vertical indicator. When it is applied to the translateral view one can accurately plot the midline retrogastric diameter at the proper vertebral level.

Now if the original postulate of Engel and Lysholm is applied it will be found to

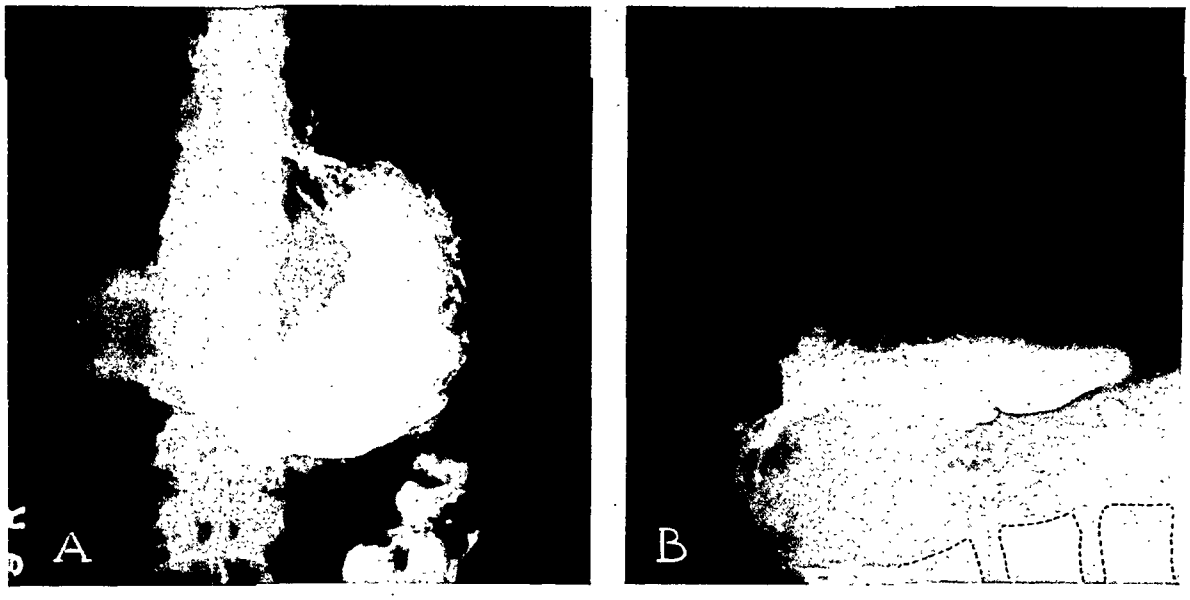


Fig. 4. This case shows no increase in the retrogastric midline diameter because the lesion does not possess any significant midline component. It does show an indenture upon the posterior wall of the stomach body and fundus, due to a cyst of the pancreatic body and tail.

be effective, i.e., "that the retrogastric soft tissues are equivalent in thickness to the anteroposterior diameter of the lumbar body at any level measured," provided one has ascertained what part of the stomach crosses the midline, at what vertebral level it crosses and then restricts the retrogastric measurement to this level only.

It must be borne in mind that the method is not infallible and that errors have been made. Holm found that extreme obesity, fat pads in the lesser sac and ascites may increase the retrogastric soft tissue measurement.

An increase in the midline retrogastric diameter cannot be translated into any one pathological entity in the absence of calcifications or other local distinguishing fea-

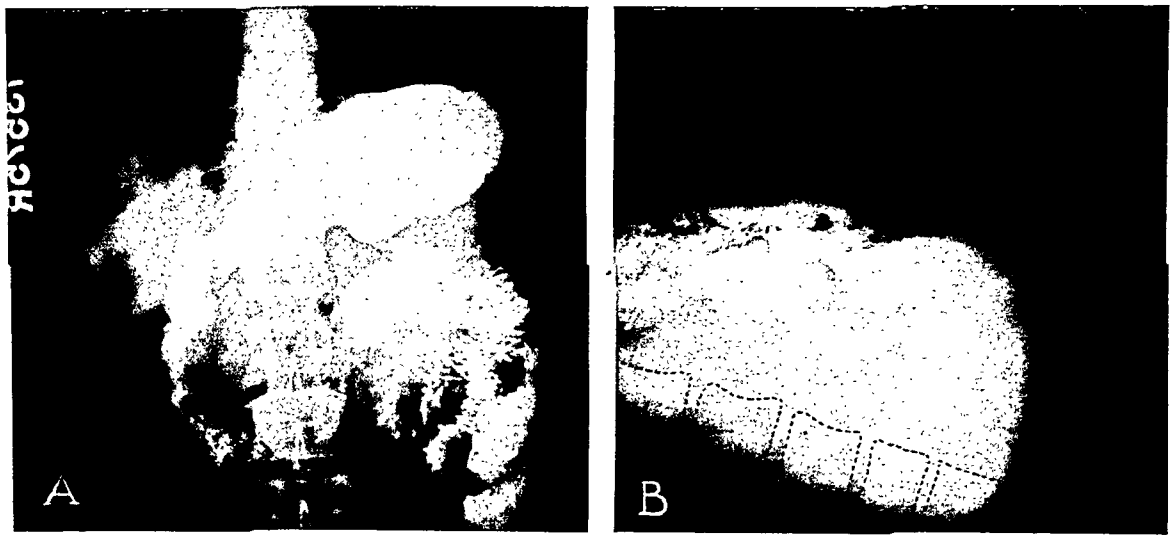


Fig. 5. This case shows an increase in the midline retrogastric diameter due to metastatic nodes from a seminoma of the testicle.

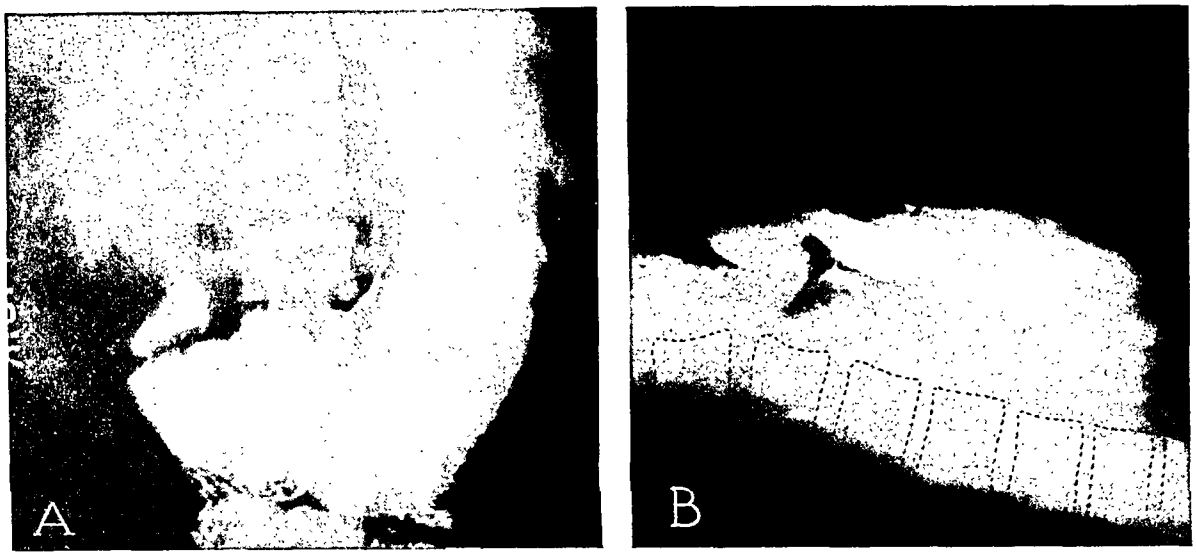


FIG. 6. This case of Hodgkin's disease shows multiple small indentures from enlarged retroperitoneal nodes upon the posterior wall of the body of the stomach, which is to the left of the midline. There is no increase in the retrogastric midline diameter because the lesion does not possess any significant midline component.

tures. The presence of disease elsewhere, as illustrated in Figures 5 and 6, aids in the correlation. Usually it simply indicates pathological enlargement of the normal regional structures (such as enlargement of the pancreas due to acute inflammation or tumor) or to the formation of adventitious extrapancreatic retrogastric mass or masses (such as retroperitoneal lymphosarcoma).

The corollary is also true that a normal midline retrogastric diameter does not exclude a retrogastric mass farther to the left. This is possible if the mass does not have any significant midline component.

At times it is not possible to obtain a midline retrogastric diameter for the simple reason that the stomach is entirely on the left. In such cases any attempt at measurement is obviously discouraged.

Likewise the presence of a localized, lobulated or generalized indenture on the posterior wall of any part of the stomach is significant in itself and does not have to be confirmed by measurements of any kind.

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BONE SCLEROSIS IN LEUKEMIA AND IN NON-LEUKEMIC MYELOSIS*

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OSSEOUS manifestations of leukemia are mostly destructive lesions. In many instances, however, bone formation prevails instead of the absorption.

The significance of pathological bone formation in leukemia is but little understood. Although extensive investigations have been carried out on bone sclerosis associated with disturbances of blood formation, these studies have been more or less limited to cases of chronic non-leukemic myelosis. In this condition massive skeletal sclerosis is frequent. Records of bone sclerosis in monocytic, lymphatic and myeloid leukemias, and in aleukemic lymphadenoses are rare.[2,3,6,8,20,40,42]

Due to the scarcity of observations and because of the light which the knowledge of bone sclerosis in leukemia may throw on similar, still unexplained, bone changes in chronic non-leukemic myelosis, a further clarification of the subject seems warranted.

The diagnostic significance of the roentgen signs must also be studied. The presence of bone changes in living persons can be diagnosed only by roentgen examination. Roentgenological findings may be decisive in cases of leukemia where results of clinical and laboratory examinations are not characteristic. In aleukemic leukemia, bone changes are suggestive before the blood or clinical picture is diagnostic.

The purpose of this article is to present roentgenological findings of bone sclerosis in leukemia and aleukemic leukemia and in non-leukemic myelosis, and to correlate them with their clinical and patho-anatomical fundamentals in a further effort to clarify the subject.

MONOCYTIC LEUKEMIA

The study of bone changes in this disease is interesting not only because of their rarity (we found only 2 records of such occurrences), but also because of the biological difference of leukemic marrow in monocytic leukemia from that in all other forms of leukemia. Bone forming impulses of the medullary parenchyma in monocytic leukemia have to be investigated on the basis of this specific biological property of monocytic proliferations (see later). We observed 3 cases of monocytic leukemia with roentgenological densities in parts of the skeleton.

Roentgenograms of our first patient (Case I) showed increased density of both humeri and femora. (We shall refer to this distribution of bone changes as "polyostotic" sclerosis.) In addition, signs of periosteal bone formation were evident (Fig. 1*A*). In our second case (Case II) monocytic leukemia was associated with a cancer of the prostate and diffuse condensation of parts of the skeleton (Fig. 2). Microscopical examination revealed that many of the bone densities were consistent with bone forming tumor metastases. Several sclerotic areas, however, contained no metastases, but monocytic proliferations intermingled with fibrosis of the marrow. In our third case (Case III) roentgen signs of diffuse densities were seen in proximal portions of both humeri and in distal areas of both femora (Fig. 3).

Microscopic studies indicated that in monocytic leukemia pathological bone tissue develops in the medullary cavity as a direct metaplasia of intercellular reticulum or collagenous structures into woven membranous bone lamellae (Fig. 1*B* and 1*C*). The fibrils, preliminary to bone formation, are furnished by cellular activity of the leukemic tissue.[27] In this regard, bone formation in monocytic and, as we shall see later, in all other forms of leukemia, is dis-

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tinctly different from bone formation in systemic and localized diseases, where bone tissue is laid down as the result of pathological activity of the osteogenic parenchyma (Paget's disease, hyperparathyroidism, bone cysts, osteogenic sarcoma, etc.). bone changes in the vicinity of destruction. Marchal, Mallet and Deprez[25] published the second recorded observation in 1945. Roentgenograms revealed large areas of bone destruction in the cranial vault. The authors considered their case a "forme os-

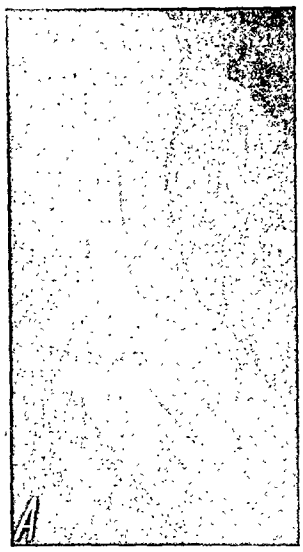
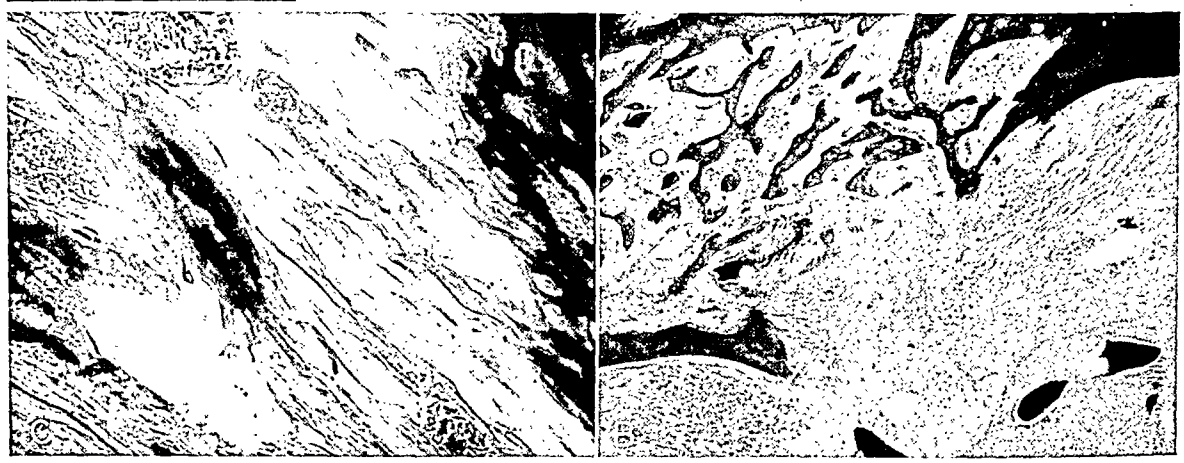


FIG. 1*A*. Case 1. Monocytic leukemia. Roentgenogram of right humerus showing thickening of cortex, periosteal bone shells, partial obliteration of the medullary cavity. B.W.F., male, aged eight weeks (No. 246224). Nodules on skin (monocytic infiltrates), hepatosplenomegaly and lymphadenopathy. Red blood cells 2.15 million, hemoglobin 6.42 gm. per cent; white blood cells 38,000, with 60 per cent monocytes, 2 per cent monoblasts, 12 per cent polymorphonuclears, 1 per cent eosinophils, 18 per cent lymphocytes, 1 per cent normoblasts per 100 white cells. Death following remarkable remission for six months.

FIG. 1*B*. Case 1. Photomicrograph ×70 from proximal metaphysis of right humerus. Van Gieson stain. Monocytic proliferation in right lower corner. Replacement of leukemic tissue by fibrous structures iu middle of photomicrograph. Destroyed old bone lamella on left lower side. Newly formed bone spicules in fibrous tissue in left upper and middle part of photomicrograph.

FIG. 1*C*. Case 1. Bone marrow in monocytic leukemia. Photomicrograph ×400, van Gieson stain. Leukemic tissue is replaced by reticular and collagenous fibers. In left upper corner and left center, thickened fibers are seen which gradually take on appearance of woven bone tissue. On right side apposition of new bone structures to older lamellae is seen.



Although bones in monocytic leukemia have not been subjected to detailed study, several authors[9,13,29] have written that bone changes may occur. To the best of our knowledge the first case was described by Kositchek[23] in 1943. Translucent bone lesions of a destructive character were seen in this case in many parts of the skeleton of a nineteen year old boy. Most translucent areas were surrounded by dense bony margins, indicating proliferating seuse de leucémie chronique à monocytes." Biopsy taken from the area of destruction revealed, however, not monocytic but lymphocytic proliferations. The bone changes in this case need further clarification.

Our Case II is similar to the recently published findings of Bersack and Feinstein.[4] In their observation osteosclerosis in a case of cancer of the prostate was partly due to focal fibrosis in the marrow. The

patient was not afflicted with leukemia. Similar observation was made in Case VI of Sussman.[35] Here a malignant pleural mesothelioma was present with generalized metastases. Bone sclerosis was not due to metastases, but to fibrosis of the marrow.

Comparing our roentgenological findings in 3 cases of monocytic leukemia with those described in myelogenous and lymphatic forms, we believe the difference is obvious. Whereas in our cases of monocytic leukemia bone formation, even though minute, is in the foreground, in other leukemias bone proliferations are exceptional. This is understandable if one considers that monocytes as well as their derivatives and leukemic tissues contributed by them, exhibit the capacity to form intercellular reticulum, while lymphoid, myeloid and erythroblastic cells do not have this inherent property.[7,11,27] Since the presence of intercellular reticulum predisposes bone formation, it is understandable why bone sclerosis is more frequent in monocytic than in all other forms of leukemia.

The number of our observations is not large enough to permit generalizations as to what extent bone formation can be considered as a characteristic feature in monocytic leukemia. Yet our microscopical studies revealed that the tissue changes in the bone marrow, which are the precursors to bone formation, are regular constituents of the monocytic form of leukemic proliferations.

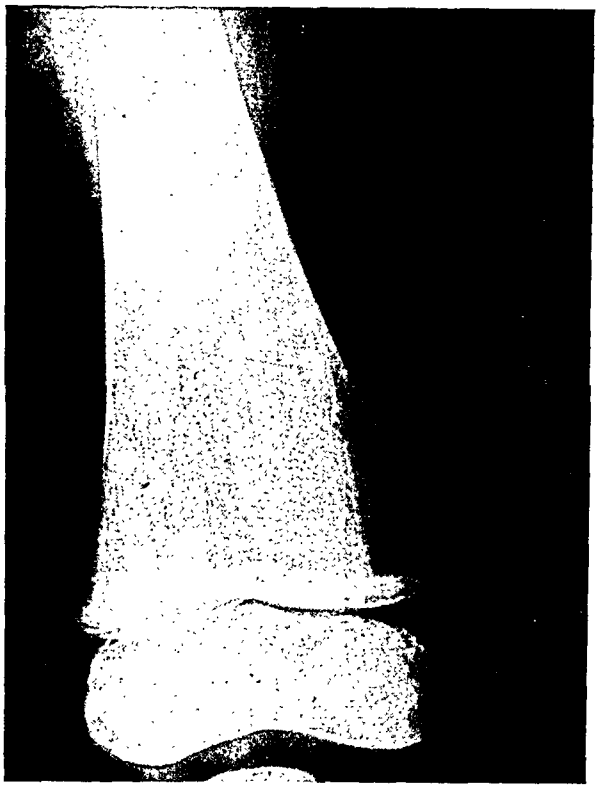


Fig. 3. Case III. Monocytic leukemia. Roentgenograms of lower ends of both femora revealed coarsening of spongy bone structures, thin cortex, increased density of medullary cavity and of lateral portions of both epiphyses. Dense transverse lines are seen in metaphyseal areas. W.T., aged three (No. A96992). Periods of lymphadenopathy, ecchymoses, hepatosplenomegaly, ulcers in mouth. Red blood cells 2.8 million, hemoglobin 44 per cent, white blood cells 27,000, with 18 per cent monocytes, 50 per cent monoblasts, 21 per cent immature stem cells, 3 per cent neutrophils and 7 per cent lymphocytes. Vital staining shows monocytic granules.



Fig. 2. Case II. Monocytic leukemia. Roentgenogram of ribs and spine. Diffuse sclerosis of eighth rib on left (see arrow). Microscopically fibrosis of marrow with monocytic proliferations. No tumor cells in this area, although patient has cancer of prostate with bone metastases. H.N., aged eighty-five (No. 27740). Prior, treated for cancer of prostate. Skin infiltrates, ulcers in mouth. Blood count: red blood cells 2.3 million, hemoglobin 34 per cent; white blood cells 66,000 with 40 per cent polymorphonuclears, 12 per cent lymphocytes, 37 per cent monocytes, and 10 per cent monoblasts. At autopsy extensive monocytic infiltrates in liver, spleen, lymph nodes, hypophysis, kidney, skin and bone marrow. Many of bony densities are tumor metastases, others (eighth rib) caused by bone formation in fibrous monocytic marrow.

It is also remarkable to realize the difference in bone changes in leukemic and aleukemic forms of monocytic leukemia. Whereas in lymphatic and myelogenous leukemias the aleukemic forms exhibit a greater tendency toward production of bone (see later), it seems that osseous changes in aleukemic reticulosis (aleukemic form of monocytic leukemia) are more frequently destructive. Further observation reveals, however, that in certain conditions bone forming properties of monocytic and histiocytic proliferations can also be demonstrated in the presence of bone absorption in hyperplastic and neoplastic lesions of aleukemic reticulo-endotheliosis.[39,40] Feher[14] presented skull roentgenograms of a child suffering from aleukemic reticulosis. A small, highly radiosensitive area of bone destruction was exhibited. However, most of the bones of the vault revealed diffuse thickening of spongy bone lamellae, producing roentgen signs of sclerosis of the diploë.

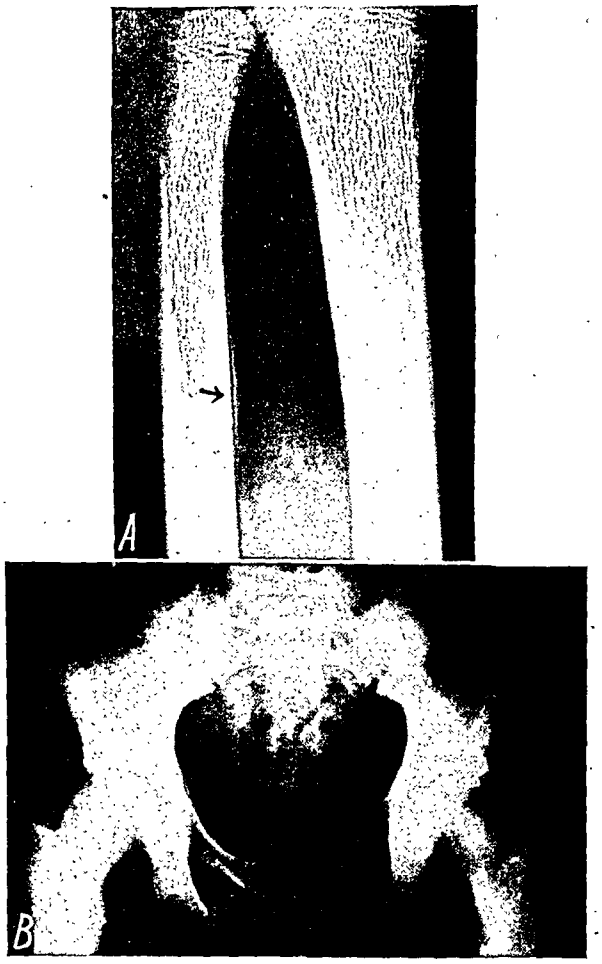


FIG. 4*A*. Case IV. Lymphatic leukemia. Roentgenograms of lower left forearm (slightly enlarged) show coarsening and thickening of spongy structures and cortex. Faint periosteal ossification on radial aspects of the cortex of radius (see arrow).

FIG. 4*B*. Case IV. Bones of the pelvis are denser than in normal conditions. Structure is somewhat irregular due to narrowing of marrow spaces and thickening of bony trabeculae. W.G.P., male, aged sixteen (No. 216040). Muscle and joint pains, splenomegaly, lymphadenopathy. Red blood cells 3.7 million, white blood cells 45,000, with 1 per cent neutrophls, 1 per cent eosinophils, 3 per cent myelocytes, 17 per cent lymphocytes, 78 per cent lymphoblasts. No autopsy.

LYMPHATIC LEUKEMIA

Roentgenological signs of bone changes exhibited in lymphatic leukemias are caused as a rule by destructive lesions. They consist of pin-point, punched-out areas in the cortex of long bones and skull, erosions at the inner aspect of the cortical layers, and transverse rarefied areas near the epiphysis. Occasionally, periosteal ossification is associated with the above changes.

Signs of bone formation are more frequent in aleukemic forms of lymphatic leukemia than in leukemic forms.[6,31,41] Bone sclerosis is very rare in the presence of leukemic lymphatic leukemia.[2,3,6,18,42]

We had the opportunity to study 5 cases of lymphatic leukemia with proliferative bone changes. In one of these instances a true leukemia was present. The four others were aleukemic lymphadenoses.

In the case of the leukemic lymphatic leukemia (Case IV), the entire skeleton was denser than normal (Fig. 4*A* and 4*B*). We propose to denominate such distributions of bone sclerosis as "panostotic" sclerosis. Irregularities of cancellous structure, spotty condensations, and coarsening of dense trabeculae were seen in vertebral bodies, pelvis (Fig. 4*B*), ribs, and long bones. Periosteal bone formation was displayed at the distal end of the left ulna (Fig. 4*A*) and of the right humerus.

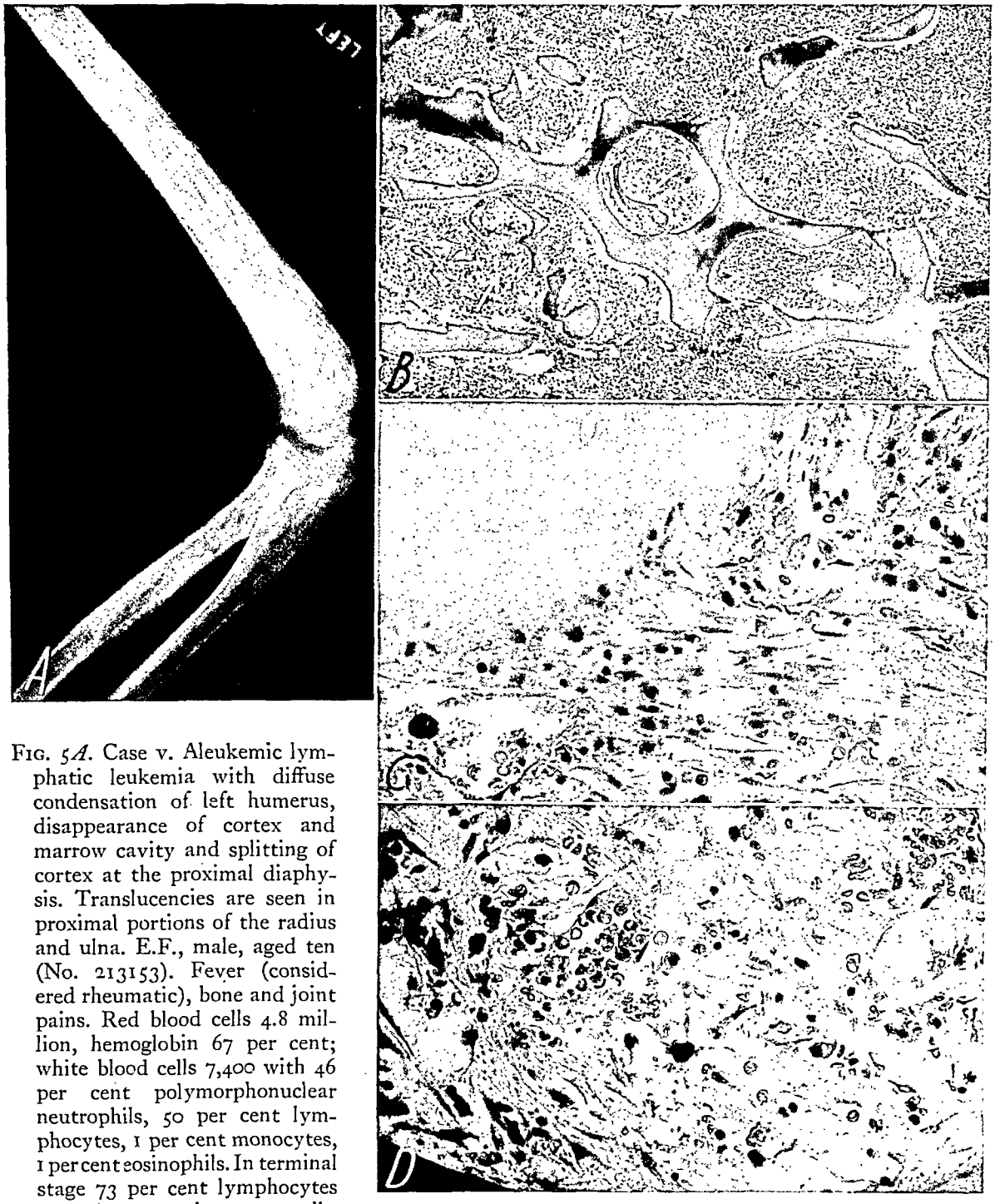


FIG. 5*A*. Case v. Aleukemic lymphatic leukemia with diffuse condensation of left humerus, disappearance of cortex and marrow cavity and splitting of cortex at the proximal diaphysis. Translucencies are seen in proximal portions of the radius and ulna. E.F., male, aged ten (No. 213153). Fever (considered rheumatic), bone and joint pains. Red blood cells 4.8 million, hemoglobin 67 per cent; white blood cells 7,400 with 46 per cent polymorphonuclear neutrophils, 50 per cent lymphocytes, 1 per cent monocytes, 1 per cent eosinophils. In terminal stage 73 per cent lymphocytes and 26 per cent immature cells, thought to be lymphoblasts. Autopsy: Many organs, including liver and spleen, are infiltrated by cells in appearance of larger lymphocytes. Many ulcers were found in the intestinal tract and a cardiac malformation was present.

FIG. 5*B*. Case IV. Fibrous aplasia of bone marrow. Photomicrograph ×75. Hematoxylin-eosin. The marrow cavity is filled by fibrous tissue contributed by fibrocytes, intercellular collagenous fibers, capillary blood vessels, mast cells, small groups of lymphocytes. Metaplastic bone formation is indicated by arrows. A few fat cells are seen in left lower corner.

FIGS. 5*C* and 5*D*. Case IV. Photomicrographs ×400. Hematoxylin-eosin. Fibrous marrow in aleukmic lymphatic leukemia. Numerous spindle-shaped fibrocytes and intercellular fibers seen in close relationship to newly formed (pink) bone structures in left center. Isolated lymphoid cells, megakaryocytes, and small cell groups are spread over the section.



FIG. 6*A*. Case VI. Aleukemic lymphatic leukemia. Roentgenogram of the distal end of the left femur (slightly enlarged), showing thickening of trabecular structure and bony proliferation in inner aspect of the cortex (on right). T.C., male, aged sixteen (No. 230239). Weakness, fever, dyspnea. Red blood cells 1.1–3.47 million, hemoglobin 20–60 per cent; white blood cells 600–2,900 with 81–88 per cent lymphocytes and many primitive lymphoblasts. Autopsy: Spleen, liver, retroperitoneal nodes, bone marrow extensively infiltrated with lymphocytes; many necroses are seen in proliferating lymphatic leukemic tissue.

FIG. 6*B*. Case VI. Aleukemic lymphatic leukemia. Photomicrograph ×75 from the lower end of the femur (hematoxylin-eosin). Marrow parenchyma replaced by leukemic infiltrates. Necrosis in leukemic proliferations in left upper corner and considerable increase of intercellular collagenous structures in center of photomicrograph. Metaplastic bone formation partly within increased intercellular fibers in right lower corner of photomicrograph.

The roentgen appearances of sclerosis in our 4 observations of aleukemic lymphatic leukemia were various.

(a) Sclerosis of a single bone (monostotic sclerosis) with splitting of cortex. Bone destruction in other bones (Fig. 5*A*) (Case V).

(b) Bony proliferations on the inside of the cortex of the femur, thickening of spongy structures at the femoral metaphysis (Fig. 6*A*) (Case VI).

(c) Sclerosis of the diploic structures on the skull intermingled with small translucencies (Fig. 7*A*) (Case VII).

(d) Circumscribed areas of bone formation in the medullary cavity of the ulna and periosteal ossification over the cortex of the femur (Fig. 8) (Case VIII).

Microscopical examination was carried out in 2 cases (V and VI) of aleukemic lymphadenosis, and in 1 case (VII) an enlarged lymph node was studied microscopically.

The histopathological appearance of osteogenesis was similar to that in monocytic leukemia. Here, too, bone spicules were formed as direct metaplasias of collagenous and reticular interstices into woven bone structures. As a result of this bone formation, the amount of spongy structures was increased.

In the sclerotic right humerus (Case V), the entire marrow parenchyma was replaced by a vascular loose fibrous tissue containing only small groups of isolated leukemic cells. The fibrous tissue was most dense about capillary blood vessels and near the cortex at the endosteum. It seemed to originate in adventitial cells of perivascular areas. There were microscopical indications that the collagenous structures were not produced by leukemic cells themselves as in monocytic leukemia (Fig. 5*B*, 5*C*, 5*D*).

In our Case VI the leukemic proliferations in the bone marrow revealed multiple areas of necrosis. In the surroundings of such necrosis, the intercellular collagenous fibers were increased and seemed to give rise to the development of bony proliferations (Fig. 6*B*).

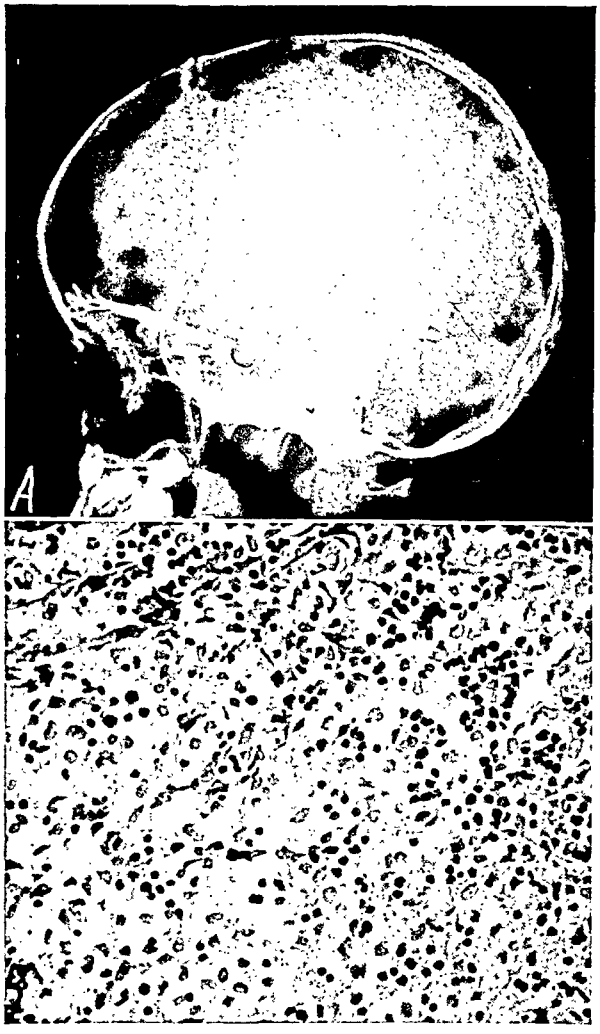


Fig. 7*A*. Case VII. Aleukemic lymphatic leukemia. Lateral roentgenogram of skull showing increased density of diploic structures alternating with faint translucencies in parietal areas of cranial vault. B.M., female, aged eight (No. 222985). Headaches, pallor, fatigue, generalized lymphadenopathy, slight hepatosplenomegaly. Red blood cells 1.5–2.9 million, hemoglobin 30–55 per cent, white blood cells 2,920–4,000 with 75–77 per cent lymphocytes, many of them immature, 22 per cent neutrophils, 3 per cent monocytes, 26,250 platelets. Lymph node biopsy shows reticular hyperplasia. No autopsy.

Fig. 7*B*. Case VII. Aleukemic lymphatic leukemia. Photomicrograph ×250 of enlarged axillary lymph node, showing proliferation of large translucent cells of reticular origin (left lower part of section) in appearance of diffuse reticular hyperplasia. Few lymphoid cells are scattered throughout the field.

Only an enlarged lymph node could be studied in Case VII. It revealed a proliferation of reticular cells intermingled with infiltrations of lymphocytes (Fig. 7*B*). Whether this appearance of the lymph node permits us to draw a conclusion as to the probable appearance of the bone marrow cannot be stated. In uncomplicated lymphatic leukemia both lymph nodes and bone marrow are simultaneously infiltrated by lymphocytes. However, in early stages of leukemic proliferations reticular hyperplasia may prevail (Stasney and Downey).

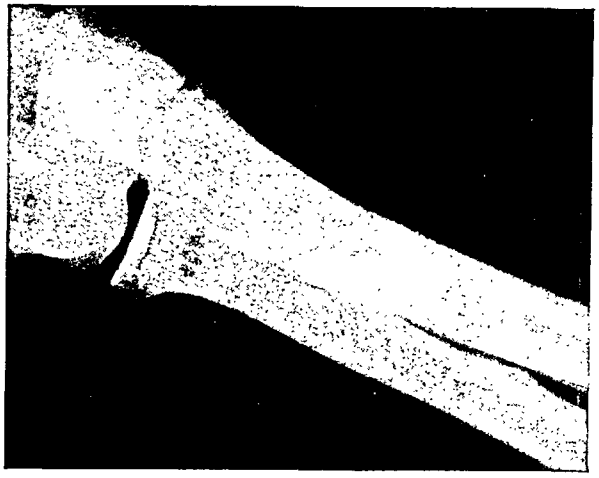


Fig. 8. Case VIII. Aleukemic lymphatic leukemia. Roentgenogram of the left elbow showing thickened cortex of the ulna and circumscribed areas of bony proliferation, obliterating a part of the medullary cavity. R.K., male, aged sixty-seven (No. 252020). Aplastic type of anemia for five years, joint pains, hematuria, lymphadenopathy, splenomegaly. Sternal biopsy shows numerous lymphoblasts. Red blood cells 2.8 million, hemoglobin 40 per cent; white blood cells 3,800 with 46 per cent neutrophils, 2 per cent eosinophils, 50 per cent lymphocytes, 2 per cent lymphoblasts. No autopsy.

When one reviews the clinical data of our observations of lymphatic leukemia, it is obvious that no relationship exists between the age of the patient, the blood count, the duration of the disease, and the type of bone changes present. The microscopical appearances were very obvious and persistent. In places in which roentgenograms revealed proliferative bone changes, microscopical study disclosed the presence of focal fibrosis or of fibrous transformation of the bone marrow of an entire bone. This is an important finding because the general opinion[31] has been that in cases of lymphatic leukemia no direct increase in connective

tissue is observed, except in the bone marrow following radiation therapy. In bones which did not exhibit osseous proliferation, the fibrosis was absent and the medullary cavity contained hemopoietic parenchyma, leukemic infiltrations, or fat or a combination of these structures,

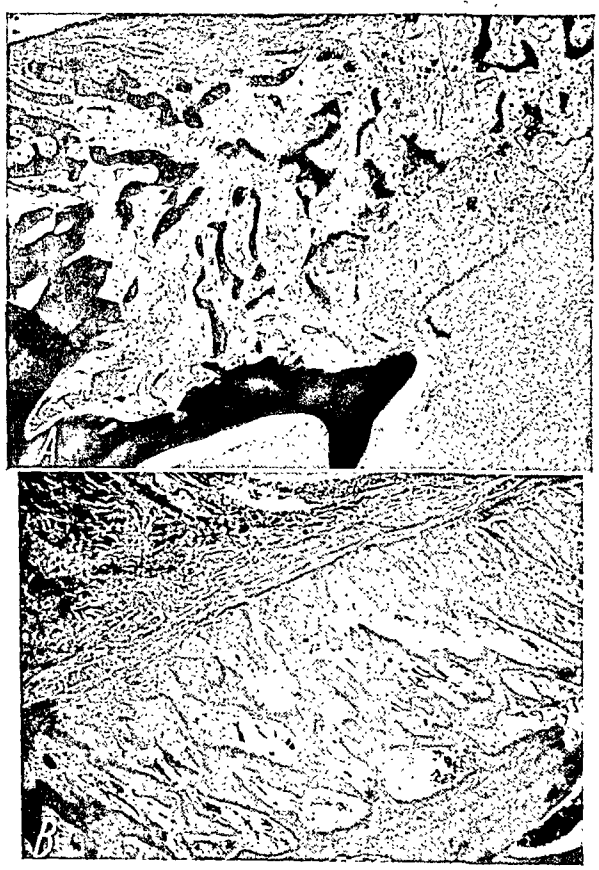


FIG. 9*A*. Case I. Periosteal bone formation in monocytic leukemia. Photomicrograph ×75. Van Gieson stain. Cortex of humerus. Leukemic proliferation in right lower corner invades and destroys bone lamellae of the cortex. Destroyed area is filled by fibrous tissue, residues of leukemic proliferations and newly formed bone lamellae in appearance of callus. Periosteum in left upper corner of section. There is no "lifting" of the periosteum seen by leukemic cells.

FIG. 9*B*. Case V. Pericsteal bone formation in aleukemic lymphatic leukemia. Photomicrograph ×75. Hematoxylin-eosin stain. Old cortex with leukemic cells in Haversian canals, right lower corner. Perpendicular bone lamellae having the appearance of callus, in middle of picture. Periosteum in left upper corner.

THE SIGNIFICANCE OF PERIOSTEAL BONE FORMATION IN LEUKEMIA

We observed this form of bone proliferation in 4 cases. In Case I, monocytic leukemia, periosteal osteogenesis was seen in most of the bones exhibiting roentgenographic densities. In Case V, lymphatic leukemia, in which the entire skeleton was denser than normal, periosteal ossification was limited to the distal end of the left radius and of the right humerus. In Case VI, aleukemic lymphatic leukemia, periosteal bone formation was intermingled with newly formed bone structures in the medullary cavity. Case VII revealed periosteal bone shells at the distal end of the left femur. In this area minute translucencies of the cortex (destructions) were seen just below the periosteal bone reaction. No translucent areas were seen in other parts of the femur.

Microscopical studies were done in Cases I and VI. They revealed that the roentgenologically seen periosteal bone shells are furnished by perpendicularly and obliquely oriented bone spicules on the outer surface of the cortex (Fig. 9*B*). (See also Kalayjian, Herbut and Erf.[21]) They developed, in our cases, in areas in which the cortex had been previously destroyed by leukemic tissues (Fig. 9*A*). Osteogenesis followed the events which take place in callus formation after injuries to bones. The callus in turn is replaced by fibrous structures furnishing the matrix of osseous metaplasia.

We failed to observe a true lifting of the periosteum by a subperiosteal accumulation of leukemic cells. This was assumed by earlier investigators.[30,35] It seemed to us that the periosteum did not present more of an obstacle to the infiltration of leukemic cells than did bone or muscle tissue. They invaded the periosteum with the same apparent ease with which they invaded the Haversian canals, perivascular spaces, bone tissue, cartilage and muscle tissue outside the periosteum. Leukemic cell groups found between newly formed periosteal bone

tissue and the cortex were in all cases small and did not impress us as being massive enough to lift the periosteum mechanically. We had to consider periosteal bone shells, in our cases, as being caused by mechanical influences (see also Caffey[6]) which followed weakening of the cortex by a large number of minimal destructions. In Case VII, such minute destructions were seen on roentgenograms as being limited to the areas of periosteal ossifications.

MYELOID LEUKEMIA

The estimation of the frequency of association of myeloid leukemia with sclerotic bone changes is difficult because in references, in many instances, non-leukemic chronic myelosis is described as myeloid leukemia.[35] In this condition bone sclerosis is frequent (in one-third of the cases). It seems, however, that there are only a few cases on record in which leukemic myelosis was associated with more or less extensive sclerosis of bones.[8,18,35] All the other observations published as bone sclerosis in myeloid leukemia were closer to non-leukemic chronic myelosis than to myeloid leukemia. In our series of 52 cases of chronic myeloid leukemia, we found destructive bone lesions 8 times. We observed no sclerosis.

The relative scarcity of observation of proliferative bone changes in myeloid leukemia is difficult to explain, if one considers that non-leukemic forms of chronic myelosis reveal rather frequent and, at times, most extensive panostotic forms of sclerosis. It is, however, reasonable to believe that in true myeloid leukemia the precursor of osteogenesis, namely, fibrosis, develops rarely. The bone marrow in this disorder usually reveals a remarkable hyperplasia of all myeloid cells. There is a more pronounced shift towards immaturity displayed than toward formation of histogenous cellular derivatives,[15] specifically collagenous and reticular fibers.

In brief, it seems to us that the reason why productive bone changes are seen so rarely in true myeloid leukemia lies in the failure of its cells to contribute to the formation of fibrous structures, and in genetic differences which are characterized by a greater tendency toward immaturity than is observed in lymphatic or monocytic leukemia. In rare instances, however, osteogenesis may occur.

Fibrosis in the marrow without sclerosis in leukemic myelosis has been repeatedly described.

CHRONIC NON-LEUKEMIC MYELOSIS

This disease differs in many features from the leukemic form of myelosis. It is characterized by a low leukocyte count, long duration, extraordinary enlargement of the spleen, immature cells of myeloid series in the peripheral blood, and an absence of the characteristic blood picture of myeloid leukemia. This condition has been associated with massive sclerosis of the skeleton in more than one-third of the observations. Such cases have been described under a large variety of denominations,* depending upon association of the disease with only fibrosis of the bone marrow or with fibrosis of the marrow and sclerosis of the bone.[1,2,19] Variation of the blood picture has also given additional incentive for variations of classification.[41] In general, cases are rare. Up to 1943, only 75 cases were listed.[32] Since that time, a number of new observations have been reported.[35] Hematological and pathological problems associated with these questions are of great complexity.

We had the opportunity to observe 2 cases of chronic non-leukemic myelosis associated with osteosclerosis in panostotic distribution.

The first observation (Case IX) is that of a male, aged sixty-two, (No. A98842). Splenomegaly was established thirty years ago. The first blood count revealing the patient's condi-

* Leuko-erythroblastic anemia with myelosclerosis (Mendeloff and Rosenthal), osteosclerosis with myelofibrosis, myelosclerosis (Vaughan), aleukemic myelosis with osteosclerosis (Hirschfeld), osteosclerotic anemia, myelosis with osteosclerosis (Hewer), myelophthisic splenomegaly (Ballin and Morse), myelosclerosis associated with leukemoid blood picture (Mettier and Rusk), chronic non-leukemic myelosis (Hickling), leukanemia (Leube and Arneth), etc.



FIG. 10. Case IX. Chronic non-leukemic myelosis. Roentgenogram of the left femur (taken 1945) showing diffuse bone sclerosis in neck and isolated areas of sclerotic foci in intertrochanteric areas. Male, aged sixty-two (A98824). Splenomegaly and anemia for thirty years (further data in text).

tion dates back fifteen years. Eight years ago an episode of polycythemia vera developed which was checked after eight months' duration by moderate doses of roentgen rays to the spleen. Characteristics which distinguished his blood picture from that of myeloid leukemia were: erythroblastosis out of proportion to the degree of anemia, and a total leukocyte count which was not as high as that seen in leukemia. At the same time the morphological pictures showed values seen in leukemia. Platelets were reduced in number and not increased as seen in myeloid leukemia with this type of morphological picture. The blood count remained essentially the same with the exception of the episode of polycythemia,* with a progressive enlargement of the spleen until the most recent examination in 1946. Comparative blood counts are recorded in Table I.

The first roentgen examination in this case was made in 1940, twenty-three years following the discovery of an enlarged spleen. At that time the roentgen appearance of the examined bones was normal (Fig. 11*C*). This, however, does not indicate that pathological changes were absent. Vaughan describes a case of panostotic sclerosis in which histopathological changes of osteosclerosis were seen, despite negative roentgen findings.

Four years later in our case, irregular densities developed in the spine, upper humeri, femora and pelvis (Fig. 10, 11*A*). They revealed remarkable progress during the following year, exhibiting finally characteristic features of massive panostotic sclerosis (Fig. 11*B*, 11*C*).

Microscopical examination of a rib (Case IX) which had been biopsied in 1944 (ST 56–756) showed a greatly thickened cortex with increase in the number and dimensions of the spongy bone trabeculae. Most of the trabeculae revealed homogeneous osteoid pink borderlines. They were frequently fused with connective fibers which filled the narrow medullary spaces. The reticular stroma appeared to originate in

* The possibility of association of erythremia with leukemia and aleukemic myelosis has led to the publication of a number of case reports[17] purporting to demonstrate this relationship. In most cases, the amount of leukemic tissue greatly exceeded the amount of erythroblastic structures, and all the pathological findings greatly resembled those characteristic of chronic myeloid leukemia.[34,35] The sequence of events, namely the polycythemia developing in a case of typical leukemia, has also been noted. Ghiron[16] observed a case in which during the course of typical myeloid leukemia the erythrocyte count increased from 2.4 million to 7.2 million and, as in our case, ruddy discoloration of the face developed.

TABLE I

Year	Red Blood Cells	White Blood Cells	Polymorpho-nuclears	Myelo-cytes	Myelo-blasts	Lympho-cytes	Plate-lets	Reticulo-cytes	Normoblasts
1930	5.0 million	19,875	70%	25%	—	17%	395,000	3.0%	5 per 400 L.
1940	8.4 million	23,000	63%	6%	8%	8%	193,000	2.4%	16 per 400 L.
1946	4.9 million	15,000	64%	17%	—	12%	12,000	—	12 per 400 L.

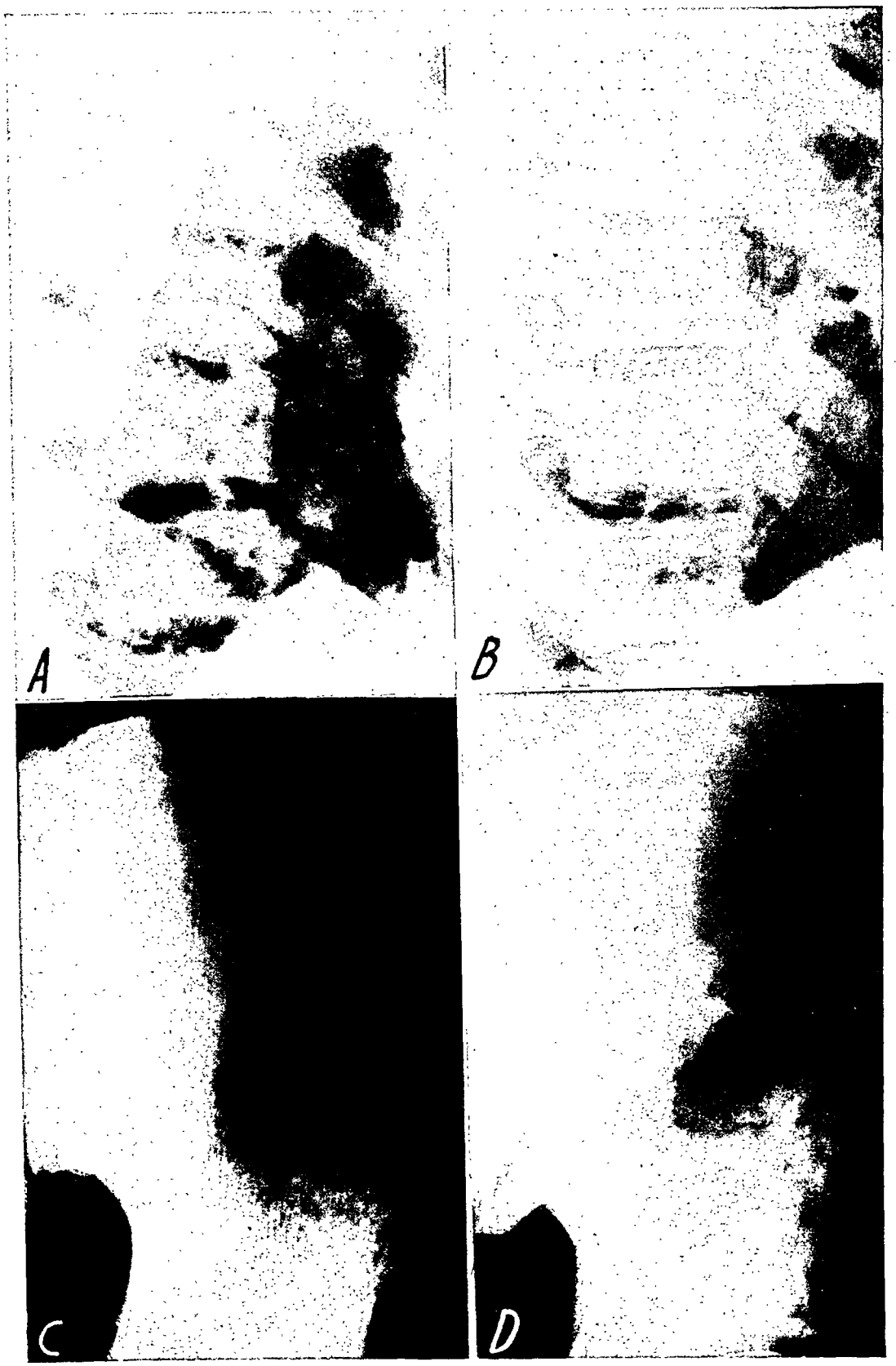


FIG. 11. Case IX. *A*, spotty sclerosis of lower dorsal vertebral bodies with coarsening of trabeculation and irregularity of structure (1945). *B*, same area one and one-half years later. Despite differences in technique, progress of sclerosis recognizable. *C*, normal appearing structure of innominate bone in 1940. *D*, same bone as in 1946, revealing fuzzy densities in lower part of the innominate bones, also in areas of the sacroiliac joint.

the endosteum. It was composed of long spindle-shaped cells. Osteoblasts and osteoclasts were absent (Fig. 12*A*, 12*B*, 12*C*).

Bone changes were almost identical in our second case (Case x) of chronic non-leukemic myelosis (Fig. 13). In this instance a male, white, American, aged fifty (E34058), came for roentgen examination because of back pains and loss of weight. Two years earlier he had been roentgenographed and diffuse density of his bones caused an erroneous diagnosis of cancer of the prostate. At physical examination a tremendously enlarged spleen and a large liver were found. The prostate showed no abnormal findings. He was fairly comfortable and worked in an industrial plant.

His blood count (August 18, 1943) was: red blood cells, 4,800,000, hemoglobin 85 per cent (Sahli), gm. 13; white blood cells 9,000, with 46 per cent polymorphonuclears (banded 40 per cent, segmented 6 per cent), 1 per cent eosinophils, 2 per cent basophils, 24 per cent myelocytes, 11 per cent metamyelocytes, 4 per cent myeloblasts, 10 per cent lymphocytes, and 2 per cent monocytes. A few nucleated blood cells were also seen.

No change had occurred in his count during the following year, after which time he felt so well that he postponed, indefinitely, any medical attention.

DISCUSSION

Clinical and hematological features were not uniform in our cases. No basic differences could be found between the symp-

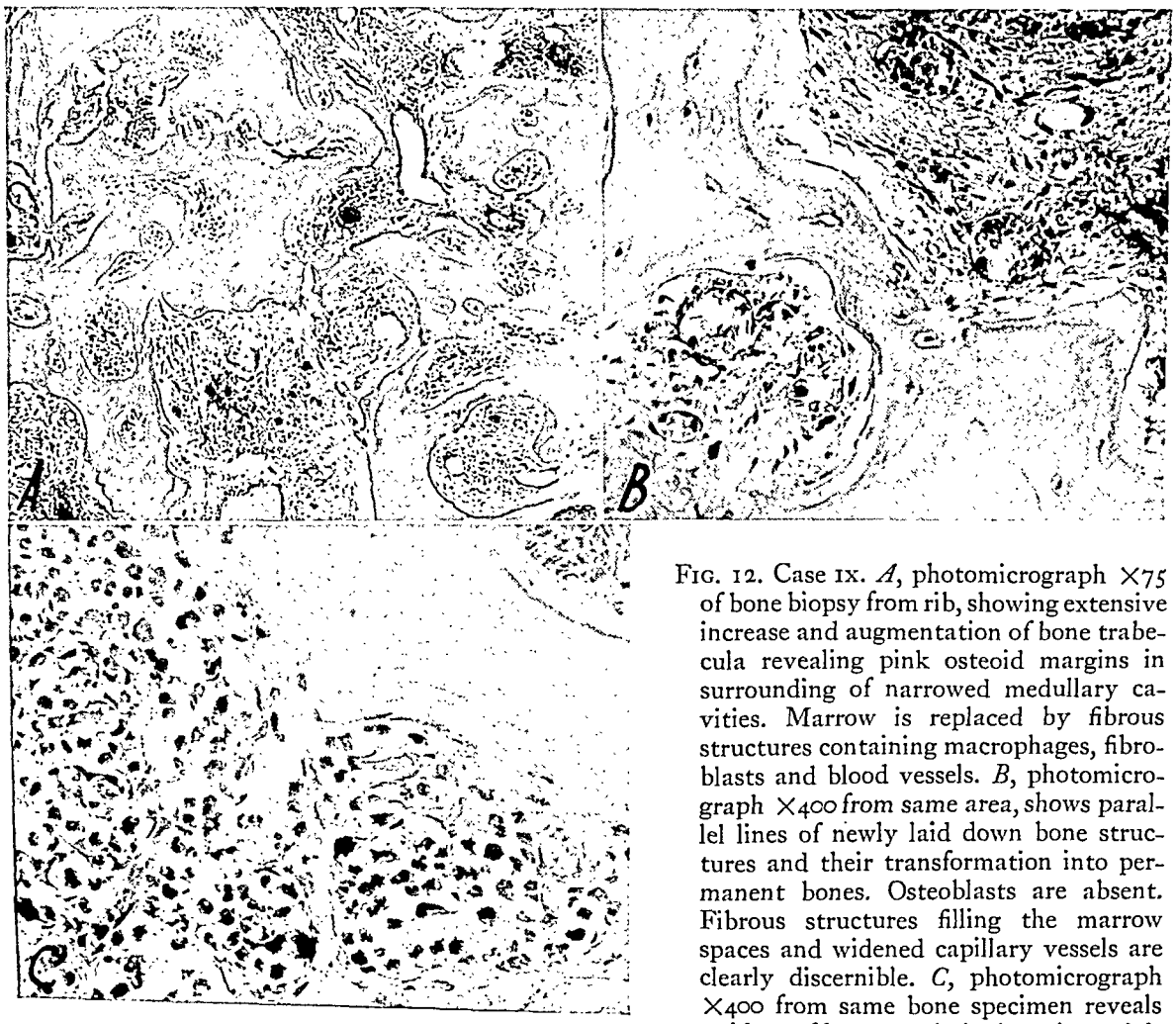


FIG. 12. Case IX. *A*, photomicrograph ×75 of bone biopsy from rib, showing extensive increase and augmentation of bone trabecula revealing pink osteoid margins in surrounding of narrowed medullary cavities. Marrow is replaced by fibrous structures containing macrophages, fibroblasts and blood vessels. *B*, photomicrograph ×400 from same area, shows parallel lines of newly laid down bone structures and their transformation into permanent bones. Osteoblasts are absent. Fibrous structures filling the marrow spaces and widened capillary vessels are clearly discernible. *C*, photomicrograph ×400 from same bone specimen reveals residues of hematopoietic tissue in medullary cavities. New formation of bone tissue is here less marked than in other areas, showing fibrous marrow. Note slight increase in reticular interstices of the marrow parenchyma.



Fig. 13. Case x. *A*, osteosclerosis in non-leukemic myelosis. Roentgen appearance of lower dorsal vertebrae. Sclerosis involves bodies, processes and ribs in male, aged fifty. Splenomegaly, leukemoid blood picture. *B*, extensive density of pelvic bones and of sacrum.

tomatology and laboratory findings in cases of leukemia with bone sclerosis and those exhibiting no signs of bone formation. Prior to the roentgenological demonstration of bone sclerosis, clinical symptoms were present on the average for three months, and the patients died usually six months after signs of sclerosis were established (disregarding our cases of non-leukemic myelosis (Cases IX and X). The spleen and liver were always enlarged. The degree of anemia varied between 1.1 million and 2.4 million red blood corpuscles (with the exception of the chronic non-leukemic myeloses in which the red blood count was approximately normal). The white blood count was never very high. It ranged between aleukemic and subleukemic counts to 50,000 white cells in those cases in which sclerosis was exhibited. Specific white cells, including immature cells, ranged from 37 per cent to 99 per cent.

The roentgenological appearance of the bones varied according to localization and structure of the densities. In 2 cases it was monostotic, in 5 cases polyostotic, and in 3 cases panostotic. In the long bones the sclerosis was characterized by thickening of the cortex and, at times, dissociation of its texture. Panostotic sclerosis was more marked in non-leukemic myelosis than in our case of lymphatic leukemia. Frequently the densities were associated with periosteal proliferations. The marrow cavity was, in some instances, entirely filled by newly formed bone tissue. This was caused either by diffuse thickening of the cortex or by development of circumscribed bony proliferations.

Differential diagnostic problems were present in Case 1 in which the possibility of congenital syphilis had to be excluded. Case X was diagnosed prior to our studies as bone forming metastases of a cancer of the prostate.

No basic differences could be observed in the histological appearance of the marrow in different forms of sclerosis. Regard-

less of whether the leukemia was monocytic, lymphatic, or aleukemic lymphatic, bone sclerosis was always preceded by fibrous transformation of the marrow. In non-leukemic myelosis the smallness of the medullary cavity produced a different distribution of collagenous fibers than was seen in other forms of leukemia. We also had the impression that the fibers were much heavier. In the case of non-leukemic myelosis, connective tissue cells were more numerous, they were spindle shaped, and lay closer to each other than in other forms of leukemia. In other words, the fibrous tissue gave the impression of being more adult and differentiated in non-leukemic myelosis than in all other forms of leukemia. Bone formation occurred as direct metaplasia of fibrous (collagenous and reticular) interstices into woven bony lamellae.

Periosteal ossification followed the pattern of callus formation. It was preceded in our cases by minute destructions of the cortex. No elevation of the periosteum itself by leukemic infiltrates was observed.

The similarity between the microscopical and roentgenological findings in leukemia and non-leukemic myelosis convinced us that in both groups of diseases the primary change seems to be the replacement of the bone marrow by leukemic proliferations. We suppose that later on the marrow of a single or of several bones becomes depopulated of its leukemic structures. In cases of monostotic or polyostotic involvements probably a local cause has to be made responsible for the development of the sclerosis. This could be localized nutritive disturbances, obliteration of nutritive arteries, etc. Following the disappearance of parenchymal cells fibrosis develops and this is the precursor of osteosclerosis.

In panostotic sclerosis, the disappearance of active marrow occurs in most parts of the skeleton and, hand in hand with this event, a progress of bone sclerosis can be observed (Case IX). Such a progression of bone changes has already been described.[35,37]

The cause of the cellular depopulation of hematopoietic and leukemic marrow in panostotic sclerosis is unknown. The theory most favored is that a toxin acts on the marrow causing fibrosis (Donhauser[10]). Mettier and Rusk[28] believe the irritation of the hyperplastic cells themselves may cause fibrosis. Vaughan and Harrison[38] point out that all the involved cells arise from the primitive mesenchymal cells of Maximov, the proliferation of which gives the sclerosing effect that results in extramedullary hematopoiesis and the special type of blood picture.

It is reasonable to believe that in panostotic sclerosis no localized causes can be considered as inducing factors for the depopulation of the bone marrow. Observations of changes of the leukemic marrow following influences of chemicals, toxins or radiation caused previous authors to believe that such factors may destroy hemopoietic as well as leukemic cells (Klemperer[22]).

Being cognizant of the progressive fibrosis of the marrow parenchyma seen in the late stages of hemolytic anemia of infants (Caffey,[6] Kraft and Bertel[24]), we present the possibility that the toxin could be related to maternal anti-Rh agglutinins produced by iso-immunization of an Rh negative mother by Rh positive fetal erythrocytes. Kraft and Bertel[24] observed recently that bone sclerosis in a late case of sickle cell anemia was very similar to that seen in the panostotic form of sclerosis in chronic non-myeloid leukemia.

We had no opportunity to carry out such tests on our patient, but we feel that studies along these lines may prove of value and contribute to the solution of some of these unsolved problems.

SUMMARY AND CONCLUSIONS

Ten cases are presented in which sclerosis of the skeleton, or of parts of it, is associated with leukemia or non-leukemic myelosis.

The series includes three cases of monocytic, five of lymphatic leukemia, and two of non-leukemic, chronic myelosis. The roentgen appearance of the bones and the significance of roentgenological features are discussed.

In five instances roentgen findings are compared with autopsy specimens of bones of the same patient. In one case bone biopsy was used for the same purpose.

The sequel of events leading to sclerosis could be reconstructed as (1) leukemic infiltration of the bone marrow, (2) disappearance of leukemic cells (depopulation of the marrow), (3) fibrosis replacing the leukemic infiltrates, and (4) bone tissue developing in fibrous areas.

Tissue mechanism: Newly formed bone lamellae develop in fibrous marrow by direct metaplasia of fibrous interstices into woven bone structures. In cases of monocytic leukemia fibrils seem to be also formed as an exoplasmatic activity of leukemic cells. In other leukemic disorders they originate from adventitial and reticular structures.

Periosteal bone shells develop according to patterns of callus formation in the presence of multiple but minute destructions of the cortex. There is no indication in our findings of lifting of the periosteum by leukemic infiltrates.

The cause for the formation of collagenous fibers, the precursors of osteogenesis, is not evident. It is, however, reasonable to believe that in cases of monostotic and polyostotic manifestations of sclerosis, local changes like nutritive disturbances may be a cause of the depopulation of the leukemic marrow. This induces the development of collagenous fibers. In our cases of monocytic leukemia, fibers are formed by the leukemic cells themselves.

In problems of panostotic involvement the authors join in the theory of Donhauser[10] who feels that an unknown toxin may give the first impulse to the development of changes leading to sclerosis. As one approach to this problem we suggest determination of the possible presence of maternal Rh agglutinins in the blood of the patient.

Practical roentgenological results and applications of these studies are:

1. Roentgenological signs of sclerotic bone changes as presented in this paper should arouse the suspicion of leukemic disorders.

2. Monostotic and polyostotic sclerosis occurs according to our observations most frequently in monocytic leukemia and in aleukemic lymphadenosis.

3. Panostotic sclerosis (entire skeleton) is most characteristic of non-leukemic myelosis. In one of our cases it occurred in lymphatic leukemia.

4. Panostotic sclerosis accompanied by great enlargement of the spleen gives a definite diagnosis of non-leukemic, chronic myelosis.

5. Splenectomy and roentgen therapy are inadvisable in cases of panostotic sclerosis. Either of them may hasten the death of the patient. Many such patients have lived comfortably for thirty years or more without such treatment.

6. Roentgenological signs of monostotic or polyostotic sclerosis in leukemia indicate the tendency of the bone marrow to become fibrous and aplastic. However, it seems to indicate no atypical course of the leukemia.

7. Periosteal bone formation in long bones is preceded by multiple, small (often microscopic), areas of bone absorption in the cortex. At times this may become visible on the roentgenograms.

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VOL. 61, NO. 1

LUMBAR INTERVERTEBRAL DISC PROTRUSION CONTRALATERAL TO THE SIDE OF SYMPTOMS AND SIGNS*

MYELOGRAPHIC VERIFICATION IN TWO CASES

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SURGICAL opinion as to the necessity for myelography in the diagnosis and treatment of protrusion of the lumbar intervertebral disc is as widely divergent as that concerning fusion of the lumbosacral spine in this condition. Bradford and Spurling[1] stated that a correct diagnosis of herniated nucleus pulposus can be made upon the basis of historical and physical findings in 80 to 90 per cent of cases and that in 50 per cent the lesion can be localized accurately to the affected interspace. Another point of view maintains that routine myelographic examination in almost all cases not only affords objective confirmation of the diagnostic impression of disc protrusion and localizes the pathology exactly, eliminating needless exploration and shortening the operative time, but reveals the presence of multiple disc herniations. Roentgenographic examination with pantopaque enabled Echlin, Ivie and Fine[2] to diagnose bilateral protrusions in 2 cases, compression of the cauda occurring at the fourth lumbar interspace on one side and at the fifth on the other. Whitcomb[3] reported 3 more such cases of bilateral herniations at different levels in the lumbar region, again diagnosed by myelography and verified surgically.

No doubt such variants of discogenic disease are in the experience of most neurosurgeons. This report is intended only to emphasize the value of myelographic investigation of patients with obvious protrusions of the lumbar intervertebral discs in revealing the unsuspected or obscure. The clinical impression in both of the 2 cases described below was that of herniated nucleus pulposus on the left, and myelograms disclosed the protrusion to lie on the right.

REPORT OF CASES

CASE 1. E. P., a railroad fireman in his late twenties, was admitted to the Illinois Neuropsychiatric Institute on July 23, 1946, because of severe pain in the left low back, present intermittently for the preceding two years, and sciatica involving the left leg, constant for the previous several days. Examination disclosed limitation of forward bending, sciatic pain on passive straight leg raising to 45 degrees, and virtual absence of the left ankle jerk. Pain was greatly increased by coughing or sneezing. There were no complaints referable to the right leg. There was a history of injury to the low back fifteen years past, and the patient had strained himself while shovelling coal very shortly before admission.

Myelography (roentgenoscopy and spot films) was undertaken, using 3 cc. of pantopaque. Much to the surprise of the examiners, a large concave, lateral filling defect was seen on the right, the side contralateral to pain and objective findings, at the level of the fourth lumbar interspace (Fig. 1). There was no defect on the left at any point.

Under general anesthesia the spines and laminae of L-4 and S-1 were exposed bilaterally. Retraction of the nerve root to the right at the fourth interspace disclosed a thin annulus which was not protruding. Incision of the membrane resulted in the obtaining of many fragments of loose cartilage. The interspace was then explored on the right (the side of myelographic defect) and a large piece of nucleus pulposus was seen to have perforated the ruptured capsule and was displacing the nerve root and caudal sac to the left.

The patient was discharged from the hospi-

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FIG. 1. Case I. A concave filling defect is seen at the level of the fourth lumbar interspace on the right. Lateral protrusion (rupture) of the intervertebral disc on the right verified at operation.

tal two weeks after operation, asymptomatic save for slight numbness of the sole of the left foot. Three weeks later he was readmitted with recurrence of the same symptoms in the left back and leg. Reoperation failed to reveal further disc protrusions at any level. A frayed left fourth lumbar nerve root was clipped and severed, and spinal fusion performed. Symptoms gradually subsided, and the patient was again discharged without complaints.

CASE II. I. R., a thirty-eight year old white farmer, was examined on May 5, 1947, because of severe pain in the left lower leg and back for the previous five months. Four years before, the patient had been struck by heavy steel wedges on the left hip. Five months prior to examination he had been lifting heavy poles, and upon straightening suddenly felt a sharp pain in the left buttock and back. Sciatica developed rapidly, but subsided during three weeks of adequate conservative therapy. The patient then returned to work on his farm. While he was plowing, excruciating pain reappeared in the left leg and persisted to a degree sufficient to prevent further activity.

Forward bending was limited to 60 degrees from the horizontal. There was paravertebral pressure tenderness from the spines of L-3 to L-5. Straight leg raising was positive at 45 degrees from the horizontal. The patient outlined an area of hypalgesia and parasthesia on the anteromedial aspect of the left thigh, knee, and upper shin. This was confirmed objectively and corresponded roughly to the third lumbar dermatome (Foerster). Both knee and ankle jerks were equally active. There were no symptoms or signs involving the right leg.

The patient was admitted to the Doctors Hospital (Washington, D. C.). Myelography



FIG. 2. Case II. A rounded, concave filling defect is seen in the pantopaque column at the fourth lumbar interspace on the right. Lateral protrusion of the disc on this side removed surgically.

(Dr. Frederick O. Coe) disclosed, instead of the expected high lumbar protrusion on the left, a consistent, concave filling defect on the right, opposite the fourth lumbar interspace (Fig. 2). The pantopaque column filled well on the left at all levels.

Lumbosacral spines and laminae were exposed bilaterally. After removal of the ligamentum flavum from the fourth interspace on the right a large protrusion of the intervertebral disc was seen. Incision of the capsule permitted the withdrawal of a sizeable fragment of loose cartilage, and much more softened disc material was removed by currettement. Exploration of the same interspace on the left (the side of symptoms) was completely negative.

Recovery of sensation on the anteromedial aspect of the left leg commenced the day of operation, and by the time of discharge (ten days postoperatively) was virtually complete. The patient declared that pain in the left testicle and groin (not mentioned during the preoperative examination) had also receded. There was never any complaint of pain in the right leg. Six weeks following discharge he remained well and asymptomatic. An island of hypalgesia was present on the inner aspect of the left knee.

COMMENT

Had operation been undertaken without myelography, the site of major pathology might not have been investigated in either of these cases. Bilateral exploration of the lumbar interspaces was performed in each, because of discrepancy between clinical and roentgenographic findings, but the disc protrusions were found only where the myelograms had indicated that they were present. Without contrast medium examination, the usual unilateral exposure might well have resulted in persistence of symptoms and signs, inasmuch as the wrong side would have been explored.

SUMMARY

Two cases of lateral protrusion of lumbar intervertebral discs on the side opposite to symptoms and signs are reported. Myelography enabled accurate exploration and removal of large herniations of the nucleus pulposus, which might have been missed had operation been undertaken upon the basis of clinical examination alone. The value of routine myelography in lumbar discogenic disease is therefore illustrated.

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BILATERAL POSTTRAUMATIC ULNOCUNEIFORM ARTICULATION

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UNDER normal circumstances the ulna does not articulate with the carpus. Its lower end, the head, articulates with the lesser sigmoid notch of the radius. The interposition of the triangular fibrocartilage prevents any direct contact with the wrist joint proper. The wrist joint is a condyloid joint in which the first row of carpal bones articulates laterally with the inferior surface of the radius and medially with the inferior surface of the triangular fibrocartilage. The triangular fibrocartilage is a somewhat pyramidal structure which is attached by its apex to a depression existing between the head and styloid process of the ulna. The apex is the thickest portion of the cartilage. From it the fibers fan out to form a broad, thin base which is inserted horizontally along the inferior margin of the lesser sigmoid notch of the radius. The lower concave surface articulates with the carpus, the upper concave surface with the head of the ulna.

Because of this anatomical arrangement the radius and the carpus form a functional radiocarpal unit, in which the carpus is dominated by the position of the radius. Rotation of the wrist follows rotation of the radius and takes place around an axis which runs from the superior to the inferior radioulnar joints.



FIG. 1. With both hands in pronation, there is seen radial deviation of the hands and prominence of the ulnar styloid.

This relationship is predicated upon the maintenance of normal length relationships between the two bones. If for any reason the ulna becomes shorter than normal and its pressure against the triangular cartilage is lost, ulnar deviation of the hand and finally corresponding curvature of the radius occurs. If, on the other hand, the radius should become relatively short, the carpus moves proximally. Because of the downward projection of the ulnar head, this is impossible and the carpus must subluxate anteriorly or radially to avoid impingement against the ulnar head. This situation commonly seen after inadequately reduced Colles' fracture has been improperly designated as posterior subluxation of the ulna.

In those cases in which the disproportion develops slowly so that the wrist can deviate radially in proportion to the growth of the ulna, the ulnar head may gradually make contact with the cuneiform bone and establish a new inferior joint about which the rotation of the forearm may take place. This is seen in those cases in which the lower end of the ulna is subperiosteally resected. As the new, plastic bone is formed, the carpus exerts a medial pressure and the lower end of the ulna deviates to the ulnar side. A somewhat similar situation is seen in the following case:

Rufus F., aged thirty-eight, presented himself in October, 1945, for a routine pre-employment examination. At this time the marked prominence and radial deviation of the hand commonly seen in malunited Colles' fracture was noted (Fig. 1). Because they so closely resembled the typical appearance of forward

luxation of the carpus, the wrists were examined for evidence of "so-called posterior dislocation of the ulna." The ulnar styloid was found to extend about 1 inch below the level of the radial styloid. It was noted with surprise that there was a practically normal range of flexion and extension of the wrist with no limitation of pronation and supination. Radial abduction was normal but the wrist could not be adducted to the midline. There was no dislocation of the ulna and no anteroposterior laxity. The patient had a powerful grasp.

The explanation of this peculiar situation became apparent when the roentgenogram was examined (Fig. 2). On both sides the radius was seen to have become relatively shorter than the ulna. The lower ends were broader than normal and were obviously irregular. The sigmoid cavity was notched and had clearly not articulated with the ulnar head for many years. As in normal instances, the carpal scaphoid and semilunar articulated with the under surface of the radius. On the right side the ulnar styloid was not united to the head, but otherwise both ulnar heads appeared to be relatively normal in outline. On both sides, however, the ulnar heads articulated with the medial aspects of the cuneiform bones which were correspondingly facetted. The hands were in radial deviation and the carpal bones showed what were considered to be configurational adaptations to their abnormal position. The lack of any limitation of rotation was obviously due to the fact that the ulna lay in the same plane as the radius and the carpal bones. The contact of the radiocarpal mass with the ulna had been simply displaced distally and instead of an inferior ulnoradial joint an inferior ulnocuneiform joint served as the fulcrum about which rotation occurred.

When the patient was carefully questioned about his condition, he recalled that as a child of ten he had fallen head first out of a tree. With his hands outstretched, the impact was received entirely on the radial epiphyses. At the time nothing noteworthy was seen and the patient was treated simply by a short period of splinting. However as the years passed he noticed gradually increasing prominence of the ulnar heads with deviation of the wrists toward the thumb side.

In all probability this patient suffered a compression of the inferior radial epiphyses. At the time of injury there was nothing to do and the child was simply splinted to relieve pain. As the years passed, the damage initially suffered by the epiphyseal cartilage resulted in retardation of radial growth and premature ossification of the epiphyseal line. The styloid process fractured at the time remained ununited while both ulnas continued to grow at their normal rates.

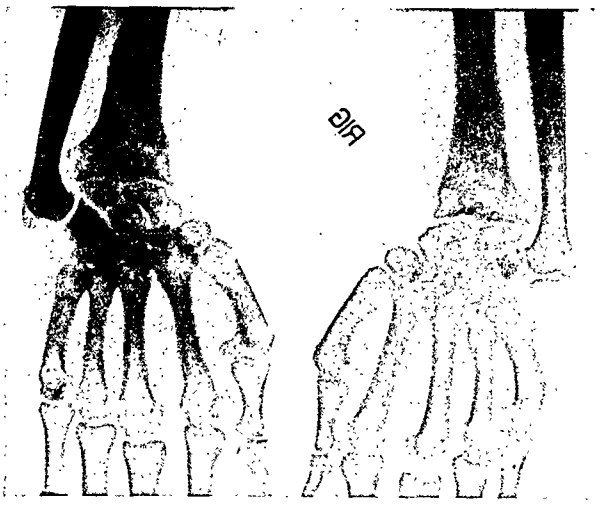


Fig. 2. Note relative shortening of both radii. The lower ends of the radii are broader than normal and somewhat irregular. On the right side the ulnar styloid is ununited. The scaphoid and semilunar bones articulate with the radius which does not make contact with the ulna at the sigmoid notch. Both ulnar heads articulate with the cuneiform which presents a well formed articular facet for their reception.

Because of the fact that ligamentous structures of the wrist were not seriously injured at the time of the injury, the ulna remained in its normal plane. As it continued to grow distally its lower end came into contact with the cuneiform and in time a facet for its reception was developed. The radial deviation of the hand was gradually accomplished by the pressure of the ulnar head, so that dislocation of the carpus did not occur, and no limitation of rotation resulted.

The patient was able to do hard manual labor without any noticeable impairment of function. The question of aesthetics did not interest him and so no suggestion of operative correction was made.

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MIXED TUMORS OF THE PALATE*

LATE RESULTS IN FIVE CASES TREATED BY TELECURIETHERAPY

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THE purpose of this report is to present the results of irradiation in 5 mixed tumors of the palate. Only 5 patients suffering from this condition were treated between 1938 and 1942. Four were treated by telecurietherapy and supplementary interstitial irradiation, and one by telecurietherapy alone. The periods of observation since treatment vary between six and nine years. The diagnosis was confirmed by biopsy in 4 cases. Four patients are well and free of disease nine years, seven years, six years and six years, and one died eight years after treatment with a recurrence that had been present for three years.

CASE REPORTS

CASE 1. N. N., male, aged forty, tumor of hard palate of eight years' duration. Examination disclosed a large ulcerated tumor measuring about 6 cm. in diameter occupying almost the entire roof of the mouth, to which it was attached by a broad base (Fig. 1). There was no



FIG. 1. Case 1. Extensive aberrant mixed salivary gland tumor before treatment.

cervical adenopathy. Biopsy showed a highly cellular mixed tumor of salivary gland type. Treatment consisted of telecurietherapy as follows: Radium content 10 grams, filtration 1 mm. platinum, distance 12.5 cm., portal 6 by 6 cm., 4,000 milligram-hours for twenty-five days (June 14, 1939 to July 21, 1939), total dose 100,000 mg-hr. The tumor dose was 1,875 gamma roentgens. All treatments were given through one right lateral portal 6 by 6 cm. There was excellent regression of the lesion over a period of approximately two months. leaving a small remnant which was treated by supplementary radiation in the form of removable platinum radium element needles as follows: Three needles each containing 2 mg. (2 cm. active length) and four needles each containing 1 mg. (1 cm. active length), filtration 0.5 mm. platinum. The seven needles containing a total of 10 mg. were inserted uniformly around the remnant and were removed after 144 hours, total dose 1,440 mg-hr., tumor dose 4,142 gamma roentgens. The interstitial irradiation was performed on September 14, 1939. The remnant regressed slowly and did not disappear entirely until May 11, 1940, approximately eight months after the radium insertion and eleven months after telecurietherapy. The patient is now free of disease more than eight years. There are no demonstrable radiation injuries (Fig. 2).



FIG. 2. Case 1. After treatment.

* From the Chicago Tumor Institute. Aided by a grant from the National Cancer Institute. Presented at the Thirtieth Annual Meeting, American Radium Society, Chicago, Ill., June 20–22, 1948.

Comment. The main point of interest in this case is the apparent cure of a very extensive, so-called radioresistant mixed tumor of the palate by intensive telecurietherapy. Another interesting feature is the slow rate of regression following treatment. On several occasions it was difficult to resist the temptation to intervene surgically and only previous experience with the slow regression of lesions of this type prevented an unnecessary surgical intervention.

CASE II. W. P., female, aged sixty-eight, tumor of the palate first noted about two months before admission. Biopsy had been performed and showed mixed tumor of salivary gland type. Examination made on June 18, 1939, disclosed a mass about 4 cm. in diameter with an ulcerated surface about 2 cm. in diameter situated in the soft palate slightly left of the midline. The lesion had the classical clinical appearance of a mixed tumor. Between May 1, 1939, and June 9, 1939, the lesion was treated with telecurietherapy through one left lateral portal 6 by 6 cm. with the following factors: Radium content 2 grams, filtration 1 mm. platinum, distance 10 cm., 2,000 mg-hr. daily for thirty consecutive days, total dose 60,000 mg-hr., tumor dose 1,448 gamma roentgens. Supplementary radium therapy was given between June 24, 1939, and July 1, 1939, in the form of a radium mold as follows: Radium content 35 mg., distance 7 mm., filtration 1 mm. platinum, surface area 7.8 $cm.^2$, 167 mg-hr. daily for seven days, total dose 1,170 mg-hr., tumor dose 2,633 gamma roentgens, total tumor dose 4,081 gamma roentgens. The lesion disappeared one month later. Approximately one year later, on May 31, 1940, interstitial irradiation was performed on a suspicious area of recurrence as follows: Four 2 mg. radium element needles were inserted for 144 hours, total dose 1,152 mg-hr. The patient remained free of disease until September, 1944, when she developed severe pain and on July 16, 1946, more than six years after the last radiation treatment, a definite recurrence was noted. Death occurred on November 9, 1947.

Comment. Because of the patient's poor general condition, the initial irradiation was discontinued after a tumor dose of 1,448 gamma roentgens had been administered. This dose proved inadequate to effect a cure although the patient remained free of disease for more than six years.

CASE III. R. McC., male, aged fifty-nine, swelling of roof of mouth for two months. A biopsy was performed and a microscopic diagnosis of adenocarcinoma was made, but a review of the sections showed a highly cellular mixed tumor of salivary gland type. Examination disclosed a freely movable, encapsulated tumor about 5 by 4 cm. in the soft palate, right of the midline. There was a linear superficial ulcer representing the site of recent biopsy. There was no cervical adenopathy. The lesion had the classical appearance of a mixed tumor of salivary gland type. The microscopic structure was essentially adenoid cystic. Treatment consisted of telecurietherapy as follows: 3,000 mg-hr. daily to each side of face (lateral portals) for twenty-two treatment days between June 17, 1940, and July 12, 1940, radium content 10 grams, filtration 1 mm. platinum, distance 12.5 cm., portals 6 by 6 cm., total dose 96,000 mg-hr. to each portal, grand total 192,000 mg-hr., tumor dose 3,109 gamma roentgens. A pronounced "epithelite" developed over the tumor about the sixteenth day. The lesion regressed slowly and on August 31, 1940, about seven weeks after the completion of telecurietherapy, a small remannt was treated with interstitial irradiation as follows: Five platinum radium element needles each containing 2 mg. of radium (active length 2 cm.), filtration 0.5 mm. platinum were inserted for 122 hours, total dose 1,220 mg-hr., tumor dose 3,812 gamma roentgens, total tumor dose 6,921 gamma roentgens. Three months later the remnant had disappeared. The patient is well and apparently free of disease at this time, about eight years after the last radium treatment, and there are no demonstrable radiation effects except a small shallow defect about 3 mm. in diameter in the mucous membrane at the site of the original lesion.

Comment. The interesting feature in this case is the intensity of the irradiation without radionecrosis and without demonstrable radiation injuries eight years after treatment. This case represents an eight year control of a moderately advanced so-called radioresistant mixed tumor by intensive telecurietherapy supplemented by interstitial irradiation. The highly cellular

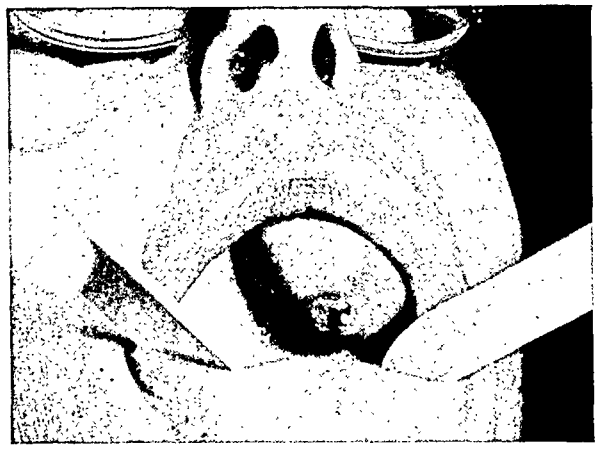


FIG. 3. Case v. Aberrant mixed salivary gland tumor before treatment.

microscopic structure places this case in Ahlbom's "semimalignant" group and originally led to a diagnosis of adenocarcinoma which was later reclassified as a cellular mixed tumor.

CASE IV. H. C., aged sixteen. On January 3, 1941, a freely movable, encapsulated tumor 2.5 cm. in diameter was enucleated from the left soft palate. Examination of the microscopic slides disclosed typical mixed tumor of salivary gland type. Examination on February 10, 1941, disclosed a local recurrence about 1.5 cm. in diameter. Treatment consisted of telecurietherapy as follows: Radium content 10 grams, filtration 1 mm. platinum, distance 12.5 cm., portal 5 by 5 cm., 10,000 mg-hr. daily for twelve treatment days given between February 10, 1941, and February 22, 1941, one left lateral portal, dose 120,000 mg-hr., tumor dose 2,820 gamma roentgens. An "epithelite" developed over the lesion about the fifteenth treatment day and a "moist epidermite" over the skin portal about the twenty-sixth day. The lesion disappeared and the patient is well and apparently free of disease six years after treatment without demonstrable signs of radiation injury.

Comment. The interesting feature in this case is the intensity of the treatment consisting of 120,000 mg-hr. in twelve consecutive treatment days without evidence of injurious radiation effects six years after treatment. This case represents a six year control of a recurrent mixed tumor of salivary gland type in a boy sixteen years of age.

CASE V. A. B., female, aged seventy-eight, growth in roof of mouth for thirty years. Examination disclosed a very extensive lesion about 7 cm. in diameter in roof of mouth with an ulcerated center about 2 cm. in diameter (Fig. 3). Treatment consisted of telecurietherapy as follows: Two grams of radium, distance 6 cm., portal 7 cm. in diameter, one hour daily for twelve consecutive days, total dose 24,000 mg-hr., tumor dose 1,233 gamma roentgens. Four months later interstitial irradiation was used as follows: Ten platinum radium element needles, each containing 1.85 mg. (filtration 0.5 mm. platinum) were inserted for 120 hours, dose 2,220 mg-hr., tumor dose 6,342 gamma roentgens, total tumor dose 7,575 gamma roentgens. The lesion regressed slowly, leaving a small fibrous mass. There is no evidence of disease six years after treatment (Fig. 4).

Comment. This is an example of an extensive mixed salivary gland tumor in a patient seventy-eight years of age controlled for six years by combined telecurietherapy and interstitial irradiation.

HISTORICAL*

Mixed tumors have been recognized for many years. The first published reports on tumors of the parotid are generally credited to C. G. Siebold[33] (1793) and J. B. Siebold[34] (1797). In 1841 A. Berard[2] published a thesis with the first attempt toward classification, and there followed a series of significant contributions, notably by Billroth[3] (1859), Bruns[6] (1859) and Virchow[37] (1863). It was soon after Minssen's comprehensive review of the subject[22] (1874) that the term "mixed tumor" became firmly established in the literature.

The first demonstration that tumors exactly resembling salivary gland tumors occurred in the palate came from Stephen Paget[27] (1886) although Robin[31] (1852) and Fonnegra[13] (1883) had already described these lesions in the palate. The French authors favored the term "adenoma" and

* In the following discussion the author has drawn freely from the excellent bibliographic review in Ahlbom's monograph.[1]

these tumors soon became the subject of numerous theses: Ott[26] (1880), Fonnegra[13] (1883), Voyer[39] (1889), Pitance[29] (1897), and more recently Nesopoulous[23] (1931) and Sapet[32] (1939). De Larabrie[8] (1890) reviewed a group of mixed tumors of the lip, mouth, and palate and applied the term "glandulae molares" thus emphasizing their glandular nature, and in 1894 Eisenmenger[10] assembled 76 mixed tumors of the palate, 5 of which he had observed personally. This author used the terms "plexiform sarcoma" and "cylindroma" commonly found in the German literature suggesting an endothelial or perithelial origin but fully recognizing their similarity with parotid tumors. Volkmann's significant contribution[38] (1895) established the endothelial conception of the origin of mixed tumors and later Gontier's monograph[15] (1904) favored the theory of an entodermal-mesenchymal origin. In 1913 Heineke[16] assembled from the literature 360 cases of mixed tumors of salivary gland and McFarland[18] in 1926 added 90 new cases. Fry[14] in 1927 published 25 cases from St. Mary's Hospital, London. In 1930 Brunschwig[7] reviewed the literature on mixed tumors of the tongue and added a case of his own.

An extensive study of mixed tumors of the palate was published by Eggers[9] in 1928 recording from the literature more than 100 cases; and in 1930 Sonnenschein[35] reviewed the literature and reported 2 additional cases. In 1931 New and Childrey[24] reported results in treatment of 48 mixed tumors of the palate seen in the Mayo Clinic between 1917 and 1930. Ahlbom's monograph[1] (1935) included 62 palatal tumors of which 22 were mixed tumors. In 1941 New and Hallberg[25] reported the end results in 76 "adenocarcinomas" of the palate of the mixed tumor type and in 1942 Martin[19] reported 103 palatal tumors of which 24 were either mixed tumors or adenocarcinomas.

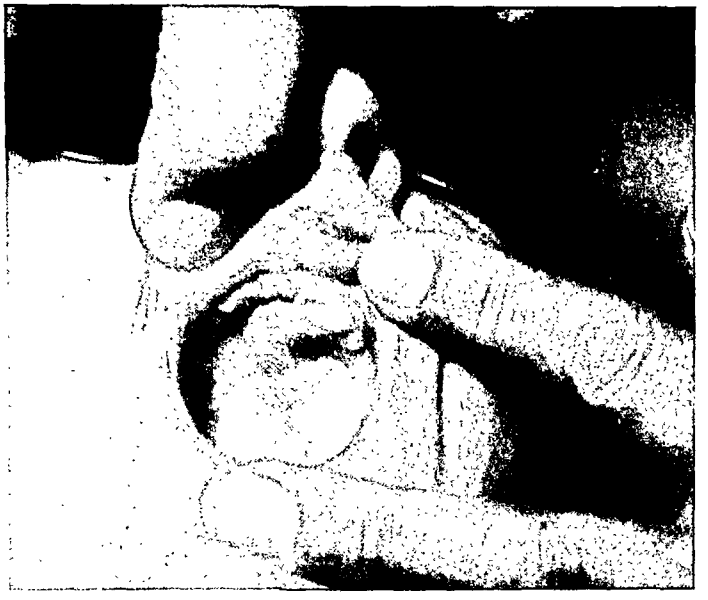


Fig. 4. Case v. After treatment.

ORIGIN

The variety of terms used to designate this group of tumors reflects the controversy relating to their connective tissue or epithelial origin and regarding their benign or malignant character. Ahlbom[1] has studied this problem extensively and includes in his excellent monograph a comprehensive review of the literature. It seems that most of the French pathologists accepted an epithelial origin whereas the German school favored the mesenchymal and later

the endothelial theory. The Cohnheim theory naturally gave rise to the embryonal doctrine. The recent tendency has been to return to the original point of view of the French school, namely that these tumors arise from the ducts or alveoli of the adult salivary glands. Certainly the epithelial origin of mixed tumors is now almost uniformly accepted (Krompecher,[17] Ewing[12]). Ewing, while accepting Krompecher's interpretation of an epithelial origin, points out that not all mixed tumors can be explained in this manner and suggests that a large portion are derived from the ducts and acini of the salivary and mucous glands and adds that the theory of branchial origin must be accepted for certain cases.

The microscopic distinction between benign and cancerous mixed tumors of the salivary gland presents serious difficulties. In the early literature the writers used the terms adenoma, epithelioma, sarcoma, endothelioma, and cylindroma without consideration as to their benign or cancerous character. Broders[5] uses the general term adenocarcinoma to emphasize their potential malignancy. In the belief that, given adequate time, all salivary gland tumors ultimately become cancerous, some writers (Boeninghaus[4]) prefer to use the term carcinoma, but Ahlbom[1] objects to this designation for a group of tumors which are mostly benign and agrees with Masson[21] (1924) in recognizing an intermediate "semimalignant" group. Reuterwall at the Radiumhemmet used such a classification on the clinical material reported by Ahlbom. Martin[19] uses the term "adenoid" tumors which he subdivides into adenocarcinoma and benign mixed tumor.

CLINICAL ASPECTS

Mixed salivary gland tumors constitute between 1 and 2 per cent of all tumors and about 5 per cent of tumors of the head and neck. They are most frequent in the parotid and next most common in the palate. They are also found in the submaxillary region, floor of mouth, larynx, pharynx, nasopharynx, tongue, upper lip, cheek, and orbit. The average age is between forty and fifty years, but they can occur in the very young. Thus Wagner's case[40] of a mixed sublingual growth concerned an infant of twelve weeks, and Pallier[28] observed one case in an infant of eleven months. The incidence is somewhat higher in women (Ahlbom[1], Martin[19]). Neither heredity nor trauma appears to be an etiological factor. In many cases the tumor had been present for many years before coming under observation, the average duration in most series being about six years. There is a wide variation in the clinical behavior. In the great majority of cases there are long periods of quiescence. Thus Pailler reported an inactive period of thirty-seven years and Wood,[41] fifty-three years. In Martland's patient[20] the growth was active for two years followed by thirteen years of inactivity. In some instances the growth is steadily progressive from the beginning.

Mixed tumors of the palate rarely cause symptoms until they reach a considerable size. Tenderness and mechanical difficulty associated with use of a dental plate often first call the patient's attention to the abnormality. Pain and bleeding are uncommon. An asymptomatic growth is not infrequently discovered by the patient's dentist. Mechanical interference with swallowing or nasal obstruction may arise when the tumor has reached considerable proportions. Large tumors may fill the mouth and extend into the antrum, nose, or nasopharynx or intracranially through the ethmoid and sphenoid bones. The anterior surface of the palate is more frequently involved than the posterior.

The clinical appearance is characteristic. The tumor is hard, round or oval, elastic, sometimes pseudofluctuating, situated usually below the surface of the mucous membrane and never exactly in the midline. The small tumors are encapsulated and freely movable under the mucous membrane; the larger ones are more fixed. Ulceration occurs late and is frequently precipitated by trauma or biopsy. As a rule, no distinction can be made between benign mixed

tumors and adenocarcinoma of the palate from clinical examination. Occasionally the more diffuse borders, early ulceration, and more rapid growth may suggest a malignant course. Rarefaction and even perforation of the bone may occur from mixed tumors of the hard palate due to pressure atrophy, a condition that is often erroneously interpreted as a sign of cancerous invasion of bone.

Upon the question of how often a benign mixed tumor of salivary gland type undergoes cancerous changes there is considerable controversy. Ahlbom contends that it is incorrect to accept a long previous history as proof that the lesion was first benign. He cites proof to the contrary by quoting examples with clinical and histopathological evidence of cancer with a long history extending back over many years (thirteen years in one case) in which microscopic examination of the original slides showed all the histopathological features of cancer.

Metastasis from mixed salivary gland tumors is infrequent and occurs late, but adenocarcinoma metastasized to regional lymph nodes in 27 per cent of Martin's cases and 29 per cent of Ahlbom's 42 mixed tumors of mouth, orbit and palate. Distant metastasis, according to Ahlbom, is estimated as 25 per cent in the entire series of cancer of salivary glands and occurs late in the course of the disease. New and Hallberg state that few of their tumors metastasized. In 13 of the 53 cases affecting the palate, cervical lymph nodes were palpable on first examination. In 4 of the 13 cases the nodes were removed and showed "adenocarcinoma" of the mixed tumor type. No mention is made of distant metastasis. Regarding systemic metastasis Martin cites the autopsy records of the Memorial Hospital containing 3 patients who died of adenocarcinoma of the palate in 2 of which there was systemic metastasis. Of 63 patients who died of mixed salivary gland tumors in Ahlbom's series 19, or 30 per cent, showed evidence of systemic metastasis. It is highly probable that distant metastasis is much more common than is generally supposed. Ahlbom estimates it as 50 per cent of those who die and 25 per cent of the entire series of cancerous tumors of salivary glands.

TREATMENT

It is generally agreed that operable mixed tumors of the palate are best treated surgically and that surgical endothermy and irradiation are valuable adjuncts. Regarding the precise value of irradiation there is some difference of opinion. Thus Martin[19] advises against its use altogether except for inoperable lesions whereas Ahlbom[1] ascribes an important role to it in operable as well as inoperable tumors. New combines radium with surgery and surgical diathermy. Most reports advocate postoperative irradiation.

In 1941 New and Hallberg[25] reported 53 adenocarcinomas (mixed tumors) of the palate of which 46 lived five or more years after treatment.* Of these 46 cases, 3 out of 7 are well after irradiation alone, 13 out of 14 after surgical diathermy combined with irradiation, and 21 out of 23 after excision and surgical diathermy (with or without irradition). Ahlbom[1] (1935), who has contributed one of the most important studies on this subject, reported 254 cases of mucous and salivary gland tumors from the Radiumhemmet (Stockholm). He omits preoperative irradiation in small, encapsulated, movable, clinically benign lesions but uses it in all other cases and especially when cancer is established or suspected. In view of the prevailing impression that preoperative irradiation complicates surgical procedures, it is interesting that Hybinnette of the Radiumhemmet (quoted by Ahlbom[1]) who has had an extensive surgical experience with these tumors, believes that preoperative irradiation helps to define the lesion and actually facilitates the operation.

Ahlbom uses irradiation alone for inoperable lesions and for operable lesions which prove to be radiosensitive. In his series one adenoma of the palate disappeared and the patient was free of disease three years and

* New and Childrey[24] had reported on group of mixed tumors of the palate in 1931 with essentially similar results.

eight months after roentgen therapy. Out of six other lesions in the "semimalignant" group, one cylindroma in the maxilloethmoidal region was sterilized by teleradium and roentgen irradiation over a period of two years and four months, one patient with "basalioma" of the hard palate was well thirteen years and five months after irradiation alone, and one fibromyxoepithelial tumor of the palate disappeared after irradiation and recurred fourteen years later. The recurrence then disappeared after a second course of irradiation. Among the 254 cases of mucous and salivary gland tumors the incidence of local recurrence was only 2.5 per cent for the benign mixed tumors and only 6 per cent when the "semimalignant" tumors are included. The author ascribes this exceptionally low incidence of recurrence to the radiation part of the treatment.

The divergent views upon the value of irradiation are due largely to the different conceptions regarding the radiosensitivity of these tumors and this leads to a discussion of the terms "radioresistant" and "radiosensitive," probably the two most confusing and misleading terms in the radiological literature. The original error which has led to this state of confusion dates back to about 1924 when microscopic studies of irradiated tissues and subsequent studies of biopsy material in relation to radiosensitivity indicated the relatively higher sensitivity of nonkeratinizing, nonsquamous carcinoma as compared with keratinizing squamous carcinoma. To these nonsquamous tumors, notably in the base of the tongue, tonsil, pharynx, etc., the term transitional cell carcinoma was applied (Ewing,[11] Quick and Cutler[30]). These studies led to the conception that squamous carcinoma was more radioresistant than nonsquamous carcinoma and, generally speaking, this holds true today. From these observations many pathologists drifted into the habit of designating any tissue which showed squamous features, microscopically, as being radioresistant so that the pathological report "squamous carcinoma, radioresistant" became routine in many laboratories. The writer confesses to being among the first to commit this error. The next source of confusion developed when clinicians, notably surgeons, began to interpret a microscopic biopsy report of "radioresistance" as indicating that the lesion is incurable by irradiation and hence should be treated surgically, and curiously enough, this view is still held by most physicians. Actually, this conception is erroneous for the following reasons: (1) The biopsy is frequently not representative of the lesion. When a tumor is composed of both squamous and nonsquamous elements, it is often radiosensitive and sometimes highly radiosensitive and radiocurable and since the biopsy frequently shows a preponderance of squamous elements, the report that the lesion is radioresistant is obviously erroneous. (2) When a squamous carcinoma is not infiltrating or only slightly so, as for example on the skin, mucous membrane of lip, mouth, or larynx, it is curable by adequate and correct irradiation in spite of the presence of squamous features in the biopsy. (3) The most important source of error is the failure to take into account the advances in radiation therapy over the years which have resulted in a better understanding of the principles and a marked increase in doses and intensity of radiation. (4) An infiltrating squamous carcinoma, incurable by external irradiation alone, may be curable by combined external and interstitial irradiation, hence a biopsy report of "radioresistance" is misleading under these conditions. (5) Anyone who has observed an extensive clinical material under radiation therapy realizes the hazard of predicting radiosensitivity in any given case, because of the numerous exceptions. Thus lesions, even melanoma which is among the most "radioresistant" tumors, may disappear completely under radiotherapy.

From this discussion it is obvious that the terms radiosensitive and radioresistant should be qualified, and the suggestion is made that they be changed to "relatively radioresistant" and "relatively radiosensi-

tive" in order to help clarify the present misunderstanding. For a comprehensive review of this problem the reader is referred to Stewart's[36] excellent article on the subject.

SUMMARY AND CONCLUSIONS

Five cases of mixed tumors of the palate were treated between 1938 and 1942. All received telecurietherapy as the essential treatment. In four cases small remnants were treated with supplementary interstitial irradiation. The disease was early in one case, moderately advanced in two and very advanced (probably inoperable) in two. One elderly patient developed local recurrence five years after inadequate irradiation* and died with disease eight years after the original treatment. The other four are living and apparently free of disease six years, six years, seven years, and eight years respectively.

Although, generally speaking, mixed tumors of mucous and salivary glands are comparatively radioresistant, there are many exceptions; furthermore the greater effectiveness of present-day intensive irradiation naturally brings within the radiocurable sphere more and more tumors formerly designated as radioresistant. The results herein reported constitute an example of this change and illustrate the fallacy of designating these tumors as being radioresistant and hence incurable by irradiation.

The excellent results of surgery and electrosurgery for mixed tumors of the palate make these procedures the methods of choice for clearly operable and benign lesions. Postoperative irradiation is an important adjunct and its use should be carefully considered in all cases and administered when clinical or histopathological evidence points to the likelihood that the operation will be followed by local recurrence. The use of preoperative irradiation should be considered in selected cases, especially in advanced lesions of borderline operability or when the age or general condition of the patient makes it preferable to avoid surgery.

The greater effectiveness of more radical irradiation makes it necessary to re-evaluate the entire problem of treatment, and since an adequate number of these tumors has not yet been treated by current techniques, an evaluation of the status of irradiation must await the late results of present methods. Since cures have been accomplished in numerous advanced cases irradiated on a palliative basis with what is now regarded as inadequate treatment, it is reasonable to expect a higher precentage of cures by more radical irradiation. These results illustrate this point. As in the treatment of all tumors each case constitutes an individual problem and the selection of the best treatment can only be made after a careful study of each patient. As regards the type of radiation, the most essential factor is that the total dose and intensity should be as large as possible without causing permanent damage to normal structures. As experience with intensive irradiation accumulates, the chances of avoiding serious complications improve and the method becomes more safe. Ahlbom points out that telecurietherapy may have the advantage of causing less injury to the normal tissues than is caused by roentgen therapy. Our experience during the last eight years with a 10 gram radium bomb† tends to support this view.

No definite conclusions can be drawn from this small group of cases. Attention is called to the possibilities of cure without radionecrosis of so-called radioresistant mixed tumors of the palate by telecurietherapy.

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* The age and infirmity of the patient did not permit adequate treatment.

† Grateful acknowledgment is made to the Union Miniere du Haut Katanga for making available the 10 gram radium bomb.

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VOL. 61, NO. 1

THE EFFECT OF HYALURONIDASE ON THE ABSORPTION OF A SUBCUTANEOUSLY DEPOSITED RADIOPAQUE SUBSTANCE*

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SINCE the discovery of the spreading factor by Duran-Reynals[1] in 1929, and its subsequent identification as hyaluronidase by Meyer, Dubos and Smyth[7] in 1936, many investigations on the biologic action of this enzyme have been conducted. Hyaluronidase activity in the skin can be clearly demonstrated by the intradermal spread of india ink,[4] certain dyes, and infections.[6] The enzymatic activity in the subcutaneous tissues, however, is less readily demonstrated. This report is concerned with the presentation of a roentgenographic method of demonstrating the absorption-hastening properties of subcutaneously injected hyaluronidase.

Favilli[2] and Sannella[10] have studied the effect of hyaluronidase on the subcutaneous absorption of india ink or saline solutions in experimental animals. More recently, Hechter, Dopkeen and Yudell[3] have demonstrated the latter effect in human infants. In these experiments estimations of rate of absorption were based upon the consistency to palpation of the injected area, the time necessary for the injection of a given quantity of fluid, and the time of disappearance of the swelling made by the injected solution.

In order to establish a more objective estimate of this absorption-hastening factor of hyaluronidase in subcutaneous tissue we have adopted a roentgenographic technique which lends itself to appraisal as readily as does the spreading of india ink in the skin. Radiopaque contrast media were injected into the subcutaneous tissues of guinea pigs, and serial roentgenograms were made to determine the time of roentgen disappearance of these substances. The time of disappearance in control animals was compared with the disappearance in animals in which the subcutaneous sites had previously been prepared with hyaluronidase. The hyaluronidase used in this study was an extract of bull testis supplied in a powder form in the strength of 50 TRU per mg.*

METHOD

Guinea pigs were tied in the supine position, and subcutaneous injections were made in the ventral body wall. The sites selected were right and left upper chest, and right and left inguinal regions. Control sites were injected with 1.0 cc. of normal saline, while test sites were injected with 12 or 50 TRU of hyaluronidase dissolved in 1.0 cc. of normal saline. Control and test sites were rotated in a clockwise manner in successive animals. Twenty minutes after preparation of the sites as above, all of these areas were reinjected with 1.0 cc. of a radiopaque contrast substance (neo-iopax, Schering, a 50 per cent solution of disodium N-methyl-3,5-diiodo-chelidamate). The twenty minute interval between preparation of the site with hyaluronidase and injection of neo-iopax is essential. When mixtures of hyaluronidase and neo-

* TRU=Turbidity Reduction Unit. One TRU is defined as the amount of enzyme per ml. which will reduce the turbidity of the substrate-protein complex from that obtained with 0.2 mg. to that obtained with 0.1 mg. substrate. The substrate-protein complex consists of a salt of hyaluronic acid combined with horse serum.[5]

* The hyaluronidase and neo-iopax were supplied by the Schering Corporation, Bloomfield, N. J.

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iopax are injected there is no absorption-hastening effect. Similar results were obtained when mixtures of hyaluronidase and diodrast were used (diodrast, Winthrop, 35 per cent solution of diiodo-pyridone acetic acid diethanolamine). Serial ventrodorsal roentgenograms were then made at ten to twenty minute intervals to record the presence or absence of radiopaque substances. Each roentgenogram usually included three simultaneously tested guinea pigs on the same 14 by 17 inch film (Fig. 1). The time of disappearance of the density due to neo-iopax was considered to be the end point (Fig. 2).

RESULTS

Ten guinea pigs were injected in a total of twenty-four sites, using either two, three or four areas in an individual animal. Of these twenty-four sites fourteen were controls, while ten were test sites. The test areas were prepared with either 12 or 50 TRU of hyaluronidase. The mean time of disappearance of neo-iopax from control sites was 113 minutes (range; 75 to 180 minutes), while the mean time of disappearance from test sites was 79 minutes (range; 20 to 120 minutes). The standard error of the mean in controls was 7.3 minutes, and in the test group 10.0 minutes.

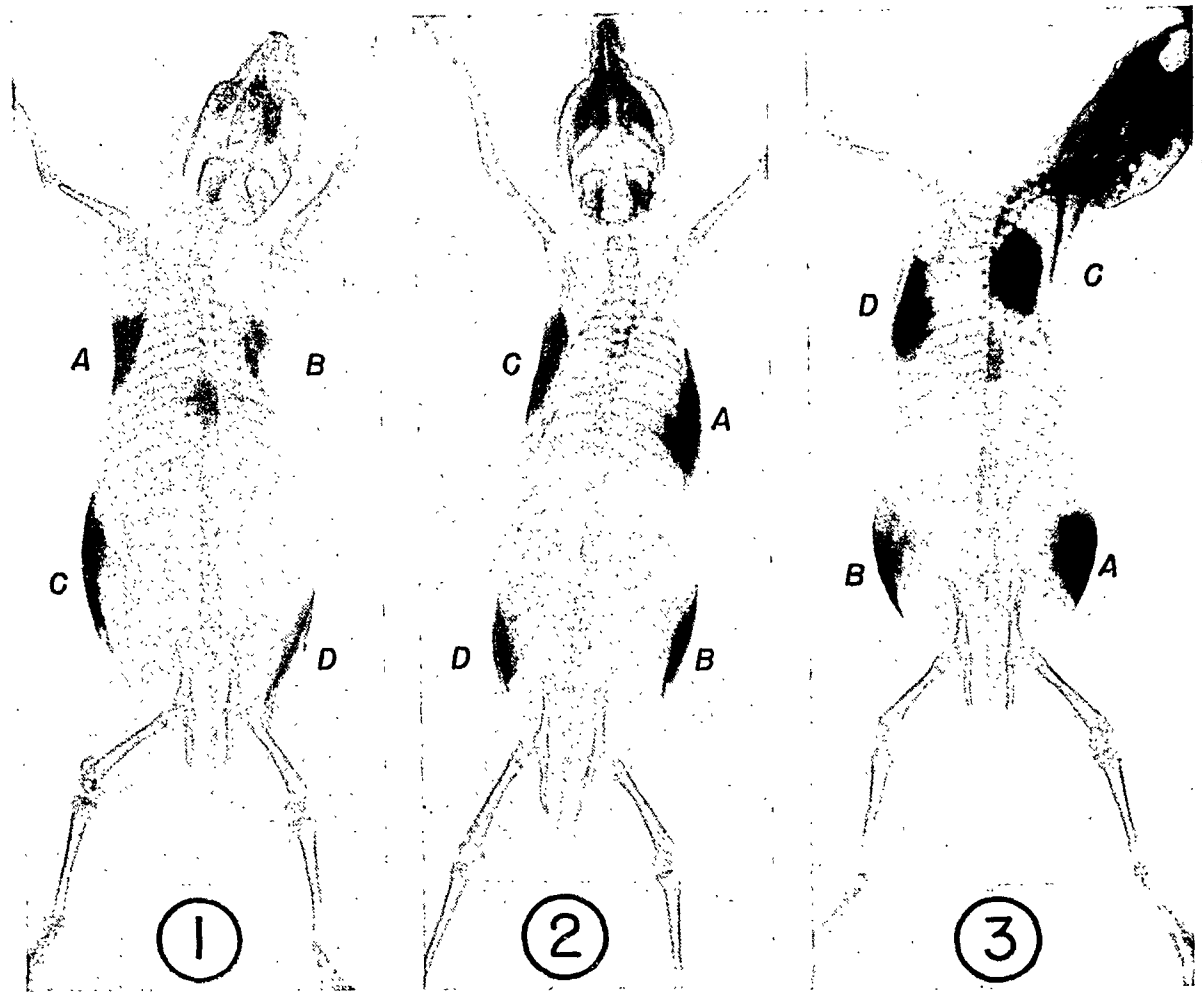


FIG. 1. Guinea pigs injected with neo-iopax in four subcutaneous sites. Preparation of each site is indicated by letters A, B, C and D adjacent to subcutaneous deposits of neo-iopax. A and D indicate controls (1 cc. of normal saline before injection of neo-iopax). Test sites labeled B were prepared with 50 TRU of hyaluronidase, and sites labeled C were prepared with 12 TRU of hyaluronidase before injection of neo-iopax. Test and control sites were rotated in successive animals as indicated.

The ratio of the difference between the mean disappearance time in test and control sites to the standard error of the difference was 2.7. This ratio indicates that the difference time is due to hyaluronidase, since the probability that it is due to random variation is less than 0.01.[8] There was no significant difference between the absorption-hastening effect of 12 as compared with 50 TRU.

mucin clot prevention, and reduction in viscosity. The present study has yielded a roentgenographic method of demonstrating hyaluronidase activity in subcutaneous tissue. This demonstration of the absorption-hastening effect of hyaluronidase uses complete disappearance of roentgen density as a definite end point. In preliminary experiments it was also found that the urinary bladder was visualized sooner in those animals in which hyaluronidase had been used to prepare the injection sites. This would seem to indicate that blood stream absorption of subcutaneously deposited substances occurs more rapidly as the result of hyaluronidase. In addition to demonstrat-

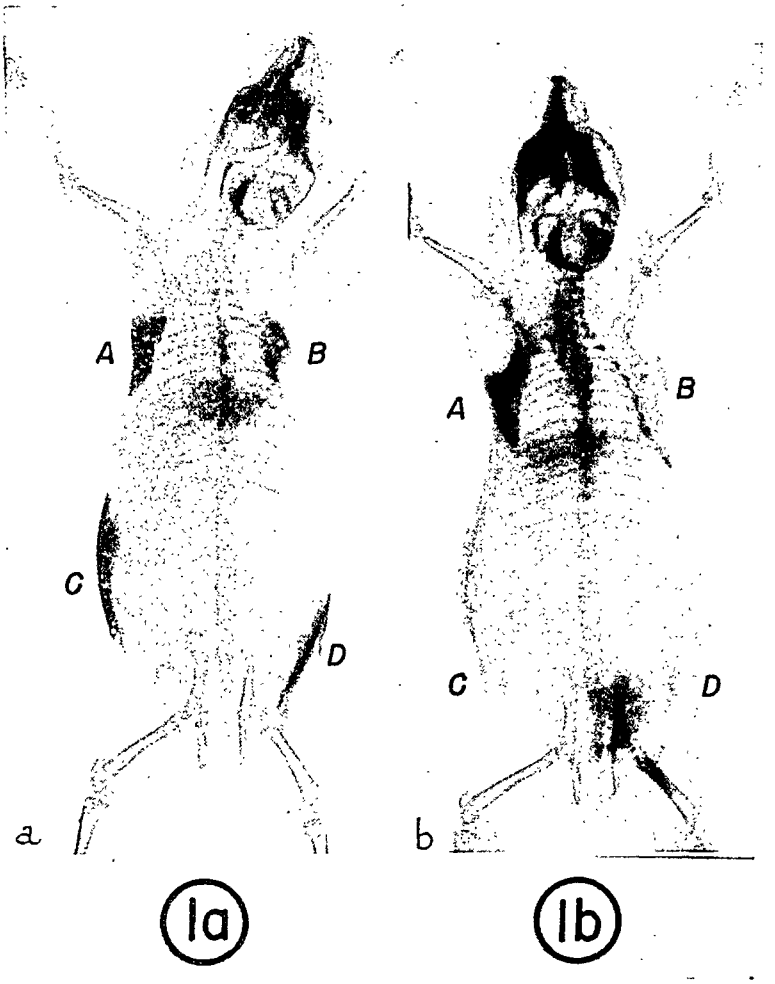


FIG. 2, *a* and *b*. Showing a guinea pig immediately after injection of subcutaneous sites with neo-iopax (*a*) and thirty minutes later (*b*). Radiopacity persists in control sites A and D, while test sites B and C show almost complete disappearance of density. Note urinary bladder density in *1b*.

DISCUSSION

Hyaluronidase activity in the skin can be demonstrated by its spreading effect on intradermally injected india ink. In vitro the enzyme activity can be measured by such chemical tests as turbidity reduction,[5]

ing hyaluronidase activity in the subcutaneous tissue, the method may be applicable in the general problem of influencing absorption from subcutaneous tissues by various chemical and physical agents.

The absorption-hastening effect of hyaluronidase may also find use in subcutaneous excretory urography in infants.[9] This may make excretory urography in infants an office procedure, rather than one requiring specialized pediatric intravenous technique.

SUMMARY

1. A roentgenographic method of demonstrating the effect of hyaluronidase on the absorption of a radiopaque substance from subcutaneous tissues is described.

2. Hyaluronidase hastens absorption of a water soluble radiopaque substance from the subcutaneous tissues.

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VOL. 61, NO. 1

EFFECT OF ROENTGEN RAYS UPON *BARTONELLA*-INFECTED AND NORMAL RATS*

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THE study reported here was preliminary to a more extensive inquiry into the effect of roentgen rays upon the course of a rat trypanosome infection. Essentially it was desired in these preliminary experiments to determine the tolerance to roentgen rays and ability to survive following irradiation of rats of different ages. However, because the stock Sherman strain animals available were frequently infected with the common rat parasite, *Bartonella muris*, it was deemed advisable to determine first whether *B. muris* infection affects the resistance of rats to roentgen rays. This was important since roentgen rays are known to have a particularly deleterious effect upon lymphoid tissue and since splenectomy enhances the virulence of *Bartonella* infection.

Accordingly, 25 rats were given single continuous exposures of from 300 to 1,000 r over the entire body; 12 of these rats were *Bartonella*-free; the other 13 were infected with *B. muris* either several days before irradiation or four hours thereafter. The physical factors used were as follows: 200 kv., 25 ma., 1 mm. Al+0.15 mm. Cu filtration, 50 cm. target skin distance. During irradiation, the animals were immobilized in lightweight cardboard boxes. Following exposure, red and white blood corpuscle counts were made and rat weights recorded, at intervals of one to two days, until death or for twenty-one days.

In all the rats, there was an initial decrease in weight and an immediate sharp reduction in the number of circulating leucocytes. Between the seventh and twelfth post-irradiation days, those rats which still survived suffered a marked drop in circulating erythrocytes. This effect on the red blood cell count was in contrast to the results of Lawrence and Lawrence[1] who noted no significant change in the erythrocyte counts of eighty-day old rats exposed to 500 r. Some of the animals which died within a week of irradiation were emaciated, had mucous diarrhea, occasionally blood-stained, and edematous eyelids. Most frequent gross postmortem findings were petechial hemorrhages in the lungs, gross hemorrhage in the stomach and atrophy of the spleen. Table 1 gives pertinent data on the red and white blood cell counts and survival time following irradiation of the two groups of rats. (The approximate normal level of erythrocytes of these rats was 8.5 million per cu.mm., and of leucocytes, 8 thousand per cu.mm.)

No definite conclusions as to the effect of *Bartonella* infection on survival time following roentgen irradiation can be drawn from the data given in Table 1. However, it would appear that *Bartonella*-infected rats are probably slightly less resistant than are normal rats to the effects of roentgen rays. It will also be noted that the larger rats survived after exposure to 300 r and 500 r for longer periods than the smaller ones exposed to 300 r and 400 r. Since the larger animals received proportionally higher dosage because of more scatter and greater absorption, it is evident that older rats are capable of sustaining

* The work described in this paper was performed in the Department of Bacteriology, College of Physicians and Surgeons, Columbia University, and the Department of Radiotherapy, Presbyterian Hospital, New York.

† The author wishes to express her thanks to Professor James T. Culbertson, formerly of Columbia University, for his guidance, and to record her appreciation of the invaluable assistance rendered by the late Doctor H. H. Kasabach and his staff, of the Department of Radiotherapy, Presbyterian Hospital.

TABLE I

EFFECT OF ROENTGEN IRRADIATION OF *Bartonella*-FREE AND *Bartonella*-INFECTED RATS

Series	Number of rats	Initial weight (grams)	*Bartonella muris* infection	Roentgen irradiation (r)	Average minimum erythrocytes (10^6 per cu.mm.)	Average minimum leucocytes (per cu.mm.)	Average survival (days)
A I[1]	1	80–140	−	300	3.2	750	21+
	2		+	300	2.2	250	21+
	2		−	500	3.0	425	18+
	2		+	500	2.3	450	20.5
	2		−	750	[3]	675	6
	2		+	750	[3]	450	4.5
	1		−	1000	[3]	250	4
	2		+	1000	[3]	150	4
A II[2]	4	36–40	−	300	3.0	560	12.5
	2		+	300	2.7[4]	550[4]	10.5
	2		−	400	[3]	[5]	4
	3		+	400	[3]	[5]	4
	12	36–140	−	+	3.1[6]	532	
	13		+	+	2.4[6]	370	

[1] Series A I: rats infected with *B. muris* before irradiation.
[2] Series A II: rats infected with *B. muris* four hours after irradiation.
[3] Rats died before fall in circulating erythrocytes occurred.
[4] Results from 1 rat only; other rat had gangrenous tail.
[5] Sufficient blood for accurate count could not be obtained.
[6] Results from rats which survived long enough for fall in erythrocytes to occur.

much larger doses of roentgen rays. Similar results were reported by Quastler[3] who found that heavier mice are less sensitive to roentgen rays than lighter mice.

Since the magnitude of the irradiation effect would depend upon the age of the animal, it was clear that absolute roentgen-ray dosage could not be used in studying the effects of irradiation on infected rats of different ages. Therefore, in order to standardize the experimental conditions, an attempt was made to determine the maximum dose which would permit survival of normal (*Bartonella*-free) rats of different ages, for twenty-one days. Forty-four rats were irradiated and weighed on alternate days following exposure (Table II).

From the results given in Table II, it is evident that the maximum roentgen-ray exposure which would uniformly permit survival for at least twenty-one days in reasonably good nutrition of rats fifteen, twenty-five, thirty-five and sixty days old at the time of irradiation was, respectively, 300, 400, 500 and 500 r. It may be mentioned that these values, at least for the oldest group, are somewhat higher than those found by Leach and Sugiura[2] who reported that all 7 of their two and one-half to three and one-half month old rats that were exposed to 500 r died within eighteen days, the shortest time interval between irradiation and death being two days.

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TABLE II

EFFECT OF ROENTGEN IRRADIATION ON SURVIVAL TIME OF RATS

Number of rats	Age when irradiated (days)	Roentgen irradiation (r)	Average number days before resumption of normal growth (wt.) rate	Average survival (days)
2	60	750	—	6
6		500	10	21+
2		400	9	21+
2	35	600	—	10
4		500	11.2	21+
2		350	5	21+
3		300	3	21+
2	25	500	—	21+[1]
5		400	5.4	21+
2		300	4	21+
2		250	3	21+
2		200	2	21+
2	15	350	—	14.5
5		300	4.4	21+
1		200	3	21+
2		150	1	21+

[1] Although these 2 rats survived twenty-one days, their nutrition was obviously seriously affected; four weeks after irradiation they had attained only slightly more than half the weight of their unirradiated litter mates.

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ON THE ASSOCIATION OF CERTAIN HEMATOMAS WITH MYELENCEPHALIC BLEBS IN THE HOUSE MOUSE*

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CERTAIN liver and testis hematomas and a case of *situs inversus viscerum* have been described by Bagg, in a series of papers, along with the kidney, eye, and foot abnormalities which are generally considered to be the expression of the gene for myelencephalic blebs. Apparently Bagg believed the liver and testis hematomas to be associated with the gene *my* for he wrote.[2]

However, as described above, disturbances have been noted, apparently mainly blood vascular in nature, in the tissues adjacent to the kidneys, and several instances have been recorded of similar disturbances, especially in the liver and testis, which are similar to the characteristic eye and foot lesions associated with blindness and club feet, respectively. These observations lead the writer to conclude that some common etiological relationship probably exists between the various abnormalities.

Grüneberg[4] discounts the association of *situs inversus viscerum* with the other anomalies but accepts Bagg's allocation of the hematomas. In the present note this latter allocation will be questioned.

The pertinent data from Bagg may be brought together as follows (Table I).

Somewhat comparable data have been obtained in this laboratory, from mice quite unrelated to Bagg's, and are summarized in Table II.

The liver and testis hematomas are visible externally in newborn mice while the pancreas hematomas and *situs inversus viscerum* can be determined by dissection only. Herein we shall be concerned with the former two anomalies only, since routine autopsies of newborn mice were not part of our experiment.

The mice with which Bagg worked were all descended from a single stock which had been exposed to roentgen radiation.[5] Grüneberg[4] is of the opinion that the original stock was already heterallelic for *my*.

TABLE I

Abnormality	No. Examined	No. Abnormal	Per Cent Abnormal	Source
Kidney defects	5600	1057	18.9	1929: 213
Eye defects	447	374	83.7	1923: 981 (Little and Bagg)
Liver hematomas	1817	7	0.4	1925: 287
Testis hematomas†	5600	15	0.3	1929: 213
Pancreas hematoma	A single case observed			1925: 288
Situs inversus viscerum	A single case observed			1924: 138 1925: 282, 297

† Bagg wrote:[3] "In one instance an animal had a hemorrhagic testis that was observed through the body wall soon after birth, and in later life it was found to have that testis completely missing." We have corroborated this observation to a certain extent with 2 newborn mice in which hematomas were visible through the body wall. These mice were autopsied at forty-two and forty-five days of age and in each the involved testis was considerably reduced (about 50 per cent from its fellow in linear dimension). Each contained motile sperm in its vas, however.

* The new data reported here were obtained incidental to work carried on for the Manhattan Project at the University of Rochester under contract number W-7401-eng-49.

Table II

Abnormality	No. Examined	No. Abnormal	Per Cent Abnormal	Origin of Mice	Method of Observation
Kidney defects	11333	10	0.1	Little *dba* × C57 Blk	Autopsy of adult ♂♂ and ♀♀
Kidney defects	164	0	0.0	Swiss × Bagg albinos	Autopsy of adult ♂♂
Eye defects	11333	12	0.1	Little *dba* × C57 Blk	Autopsy of adult ♂♂ and ♀♀
Eye defects	164	0	0.0	Swiss × Bagg albinos	Autopsy of adult ♂♂
Liver hematomas	19514	22	0.1	(Little *dba* × C57 Blk) × (Swiss-Bagg albino)	External examination of newborn mice, ♂♂ and ♀♀
Testis hematomas	19514	38	0.2	(Little *dba* × C57 Blk) × (Swiss-Bagg albino)	External examination of newborn mice, ♂♂ and ♀♀
Pancreas hematomas	>100	0	—	(Little *dba* × C57 Blk) × (Swiss-Bagg albino)	Autopsy of newborn mice, ♂♂ and ♀♀

After the anomalies appeared the mice were selectively inbred for the defects and undoubtedly they were made homozygous for *my*.

Our material is thought to be free of *my*. Our mice are unrelated to Bagg's *my/my* mice; they originated from well-known stocks in which *my* has never been reported; and they have practically none of the kidney and eye defects associated with the gene (compare Tables I and II).

Comparison of the frequencies of testis hematomas in Table I and Table II gives a chi-square of 1.10 with one degree of freedom (P ca. 0.25), and suggests a low occurrence of testis hematomas in mice *regardless* of the presence of the gene for myelencephalic blebs.

However, the comparable values for the liver hematomas do not support a similar conclusion. Here the chi-square value of 9.09 with one degree of freedom ($P < .01$) is consistent with an association of these hematomas with *my*.

Since our +/*my* mice exhibit frequencies of the testis hematomas similar to those of Bagg's *my/my* mice, it appears likely that testis hematomas (and probably pancreas hematomas and *situs inversus viscerum*) are not always to be attributed (either directly or indirectly) to the gene *my*. The data do not support such a conclusion regarding liver hematomas although it is not unlikely that strain differences, independent of *my*, may be chiefly involved.

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DEPARTMENT OF TECHNIQUE

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A NEW PROCESSING ROOM ACCESSORY: THE "CLIP DRIP" TRAY*

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BALTIMORE, MARYLAND

NO single problem is so commonly and universally encountered as that of how to best handle wet films brought from the processing room for emergency viewings. The problem is greater in the larger hospitals where the intern, the assistant resident, and the resident of a service, each in turn and at separate intervals is apt to arrive at the roentgen department and express his desire to review the "wet" films. Processing solutions, water, or combinations of both, drip from the film as they are carried from the dark room to the roentgenologist's viewing boxes. The floors are dripped upon, the viewing box shelf and any films thereon are dripped upon, and the roentgenologist's clothes are dripped upon—in fact everything but the drip cloth which is supposed to be held under the wet films bears the tell tale stains of this roentgenological industrial hazard. It occurred to the author that the solution to the problem would be a tray that would "clip" the drip. After considering various materials, "Lucite" was selected because of: (1) its resistance to water and developing chemicals; (2) its tensile strength and non-breakable qualities; (3) its light weight.

A tray was then designed and early this year one of the larger manufacturers (DuPont) fabricated samples (Fig. 1). Several trays are kept in the processing room. When a wet film is requested, a tray is snapped onto the lower bar of the film hanger (Fig. 2). The hanger may now be

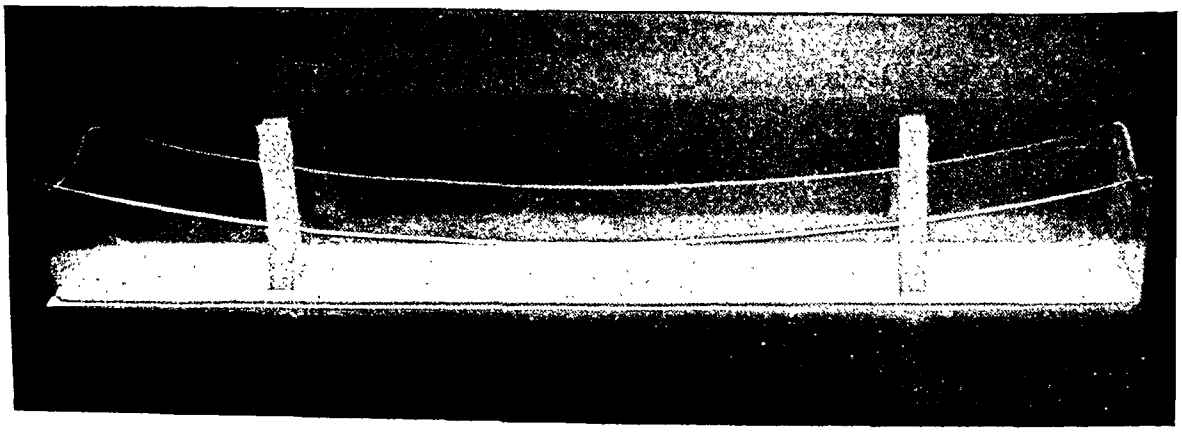


FIG. 1

*Patent pending.

lifted, tilted, or swung about. The dripping solutions are caught in the tray. When the film is held in front of an illuminator the tray holds the bottom out far enough so that the wet film does not touch the glass. The tray has been tested under actual working conditions in the Department of Radiology of a large city hospital. It has proved completely satisfactory and is therefore being described here. It has proved of special value in carrying wet films into the operating room during orthopedic operations.

SUMMARY

A tray has been designed and fabricated for the purpose of catching dripping solutions from "wet films."

2307 Crest Road
Baltimore, Maryland

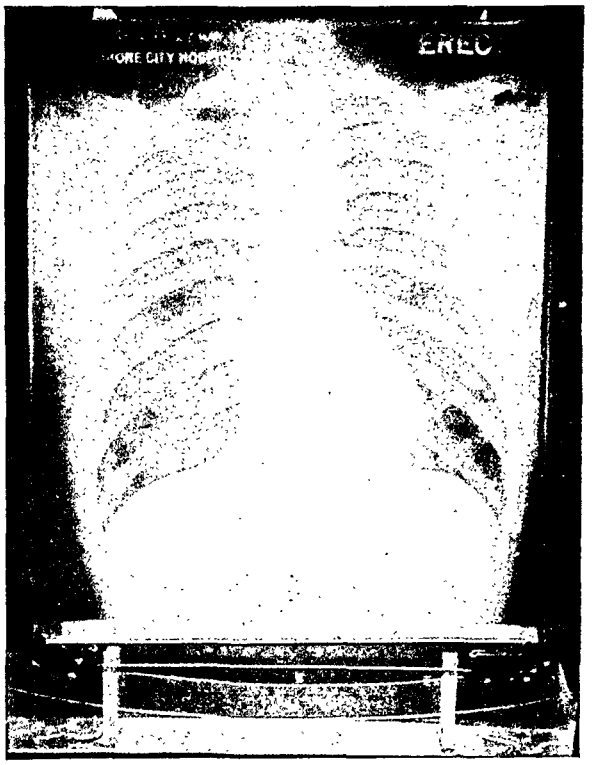


Fig. 2

TRIFOCAL GLASSES AS AN AID TO THE OLDER ROENTGENOLOGIST

By RAMSAY SPILLMAN, M.D.
NEW YORK, NEW YORK

AT about the age of forty-five, the eye of the average human being has acquired a focal length that is a little longer than his arm. Among the many inventions of Benjamin Franklin, the bifocal spectacle was no mean achievement. Some persons have more trouble adapting to it than others.

In the early fifties, presbyopia has normally increased to the degree that an

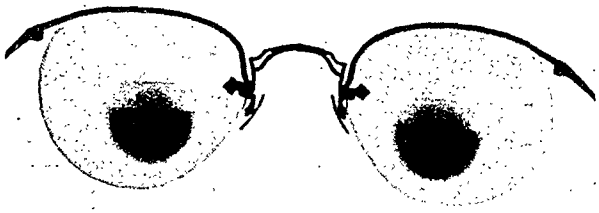


FIG. 1

adequate addition for reading differs so greatly from the correction for distance that there is an intermediate zone in which sharp vision is not obtained. This zone includes the distance at which one would normally read roentgenograms.

For persons who can accept them, trifocal glasses bridge this gap and give continuous vision. The only reason for this communication is that I find comparatively few of my colleagues in the age group to benefit from them have ever heard of them. The principle is simplicity itself, though the optical details inspire appreciative admiration. The lens is ground to uniform curvature, the difference in the strength being inherent in the different indices of refraction of the three kinds of glass involved. The accompanying roentgenogram (Fig. 1) illustrates the principle and also shows the pattern formed by the three elements. The intermediate rectangle constitutes an addition that is half the strength of the lower addition. I have found that the proper inclination of the head to throw the vision through the needed correction very quickly becomes a reflex action and involves no conscious effort; and this, notwithstanding a complicated optical prescription involving spheres, cylinders, and prisms.

115 East 61st St.
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Thirty-first Annual Meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

EDITORIALS

NITROGEN MUSTARD THERAPY

SHORTLY after World War I a few articles[1,2] appeared in the medical literature pointing to the fact that the mustard gas used in chemical warfare exerts, among other things, a toxic effect on the hemopoietic system leading to leukopenia. During World War II research carried out on a series of mustards revealed that most of these compounds also produce a cytotoxic action on the elements of the lymphoid system and to a certain extent on the proliferative processes of malignant neoplasms. This action in many ways resembles that observed following roentgen irradiation. Hence, several investigators turned their attention to the possible therapeutic applicability of some of the mustards.

Gilman and Philips,[3] in 1946, gave the first account of such applicability. These authors reviewed considerable unpublished work carried out in conjunction with the war effort and analyzed the relation existing between the chemical constitution and the biological action of numerous nitrogen mustards. They arrived at the conclusion that there is an almost infinite variety of mustards which may be prepared and that considering the great selectivity of action of some of these drugs "a measure of optimism is lent to the anticipation of future investigations." Bearing out this prediction of Gilman and Philips, during the next two years a relatively large number of articles were published in rapid succession.

It may not be out of place, therefore, to try to analyze some of the progress made and to consider the present status of the medical usefulness of the mustards.

The clinical and pathologic effects were studied in extenso recently by Graef, Karnofsky, Jager, Krichesky and Smith.[4] One sulfur and four nitrogen compounds were investigated which by using the official War Department symbols for brevity were designated, as H (bis-β-chloroethylsulfide), HN_1 (ethyl-bis-β-chloroethylamine), HN_2 (methyl-bis-β-chloroethylamine), HN_3 (tris-β-chloroethyl-amine) and TL_{301} (iso propyl-bis-β-chloroethylamine). Of the five preparations HN_2 is the most commonly used in clinical therapy and is thus of particular interest as far as this review is concerned.

Graef and his colleagues undertook their investigations principally on rodents (albino mice, albino rats and New Zealand rabbits) and on some dogs but they also correlated the data available on other species. It was demonstrated that sulfur and nitrogen mustards given by different routes of administration absorbed readily, inducing injury to the lymphatic tissue, spleen, bone marrow and epithelium of the small intestine, and, if the dose was large enough, death of the animal. In general, the destructive action and the extensive alterations produced showed an extraordinarily close parallelism to the well known effects of the direct application of the roentgen

[1] Krumbhaar, E. B. Role of the blood and the bone marrow in certain forms of gas poisoning. *J. A. M. A.*, 1919, *72*, 39–41.

[2] Pappenheimer, A. M., and Vance, M. The effects of intravenous injections of dichloroethylsufide in rabbits with special reference to its leucotonic action. *J. Exper. Med.*, 1920, *31*, 71–94.

[3] Gilman, A. and Philips, F. S. The biological actions and therapeutic applications of the B-chloroethyl amines and sulfides. *Science*, 1946, *103*, 409–415; also, Philips, F. S., and Gilman, A. The relation between chemical constitution and biological action of the nitrogen mustards. Approaches to tumor chemotherapy. Am. Assoc. Advancement Sc., 1947, pp. 293–305.

[4] Graef, I. Karnofsky, D. A., Jager, V. B., Krichesky, B., and Smith, H. W. The clinical and pathologic effects of the nitrogen and sulfur mustards in laboratory animals. *Am. J. Path.*, 1948, *24*, 1–47.

rays. The authors stress, however, that for the moment, this parallelism must be regarded as only superficial since in neither case has the fundamental mode of injury been determined.

Gilman and Philips[3] in describing the pharmacology of the nitrogen mustards consider that the presence of the imine ring is important in endowing the compound with cytotoxic activity. However, the specific sites of action of the imine ring are dependent upon the rate of intramolecular cyclization of the parent substance and the formation of the imonium moiety. The end result is complete dissolution of the cell if the dose is large and varying degrees of growth inhibition if the dose is smaller.

Fell and Allsopp[5] studied the action of mustard gas ($\beta\beta'$ dichlorodiethylsulphide) on living cells in vitro by using as cultures small pieces of choroid and sclerotic from ten to twelve day chick embryos grown by the hanging drop method. It was noted that liquid mustard gas or its concentrated vapor immediately coagulated and killed living cells with little distortion of form. Low concentrations of mustard gas vapor led to slow death of the cells with disintegration of the cystoplasm associated with enormous distortion of the cell outline, of the chromosomes in mitotic cells and of the chromatin structure of resting nuclei. Cells grown in sublethal concentration of mustard gas showed many abnormal mitotic figures.

The histopathologic effect of the nitrogen mustard (HN_2) on tumors and other tissues in the human was analyzed by Spitz.[6] This author during a period of two and one-half years performed postmortem examinations in a group of 57 cases which were treated at Memorial Hospital principally with nitrogen mustard after other forms of therapy, including external irradiation, became no longer effective. The cases represented 12 of Hodgkin's disease, 16 of lymphosarcoma, 9 of lymphatic leukemia, 7 of myelogenous leukemia and 13 of a variety of malignant tumors.

The changes observed on the neoplastic tissues were, curiously, most pronounced in the lymphosarcomas although the most encouraging clinical results have been obtained in Hodgkin's disease. These changes consisted of ballooning of the cytoplasm by fat and of swelling with loss of chromatin pattern of the nuclei. They were attributed to the direct effect of the nitrogen mustard since no other known condition would lead to such accumulation of the lipid material. The destructive phase persisted for as long as twenty-one days following therapy in lymphosarcoma but in Hodgkin's disease it was not evident after an interval of eight days. In most cases, after this period, there was a transformation of the original tumor into one of steadily decreasing cell population with increased pleomorphism of the remaining cells, multinucleated giant cells making their appearance quite frequently. Not all cells were affected equally and some escaped injury altogether. In the lymphatic leukemias no cytologic alterations were observed; there was simply a reduction in the number of cells comprising the leukemic infiltrate. The myelogenous leukemias, except the acute cases, remained uninfluenced by the nitrogen mustard gas therapy. Likewise no cytologic effect was noted in a variety of malignant epithelial tumors.

Of the normal tissues, Spitz found changes attributable to the nitrogen mustard therapy in the bone marrow and the testes. The alterations of the bone marrow consisted of hypoplasia, disappearance of the granulocytes and persistence of a few erythroblasts and megakaryocytes. In the more severe cases hemorrhage, edema and diffuse myxomatous changes were also present. In general, the degree of hypoplasia of the bone marrow depended on the total cumulative dose and the interval following therapy. The effect noted in the testes was rather surprising. In no less than

[5] Fell, Honor B., and Allsopp. C. B. The action of mustard gas on living cells in vitro. *Cancer Research*, 1948, *8*, 145–161.

[6] Spitz, Sophie. The histological effects of nitrogen mustards on human tumors and tissues. *Cancer*, 1948, *1*, 383–398.

90 per cent of the cases examined a moderately advanced atrophy developed from which recovery seldom occurred. By comparison, testicular atrophy was found in only 38 per cent of miscellaneous malignant tumors and 57 per cent of malignant lymphomas and leukemias not subjected to mustard but to other forms of therapy. Spitz also made the important observation that in contradistinction to animal experiments the mucosa of the gastrointestinal tract of the human exhibited no unusual alterations, regardless of the amount or duration of the nitrogen mustard therapy.

The clinical value of nitrogen mustard therapy was studied by a number of investigators. Because of the above enumerated reasons, Hodgkin's disease, lymphosarcoma, the leukemias and a few other types of malignant neoplasms were chosen as most suitable for treatment. In the great majority of cases reported in the literature HN_2 was used. The average dose amounted to 0.1 mg. per kilogram of body weight which was repeated daily, for four to six doses. The drug was prepared fresh and to avoid local thrombosis it was injected within five minutes into the tube of a saline intravenous system already in operation. After intervals of two to three months further courses of treatment were given, depending on the symptoms of the patient.

Recently, Wintrobe and Huguley[7] dealing with a larger series of cases have critically evaluated what one may expect from such a procedure. These authors treated with HN_2 a total of 102 cases and have observed the response for periods of three to thirty-three months. They have also analyzed for the purpose of comparison the available cases from the literature. The best results were obtained in Hodgkin's disease. A regression of the tumefactions, splenomegaly, fever, bone pain and various other clinical symptoms was noted lasting repeatedly over periods of many months. In view of the fact that most of the cases treated were already radiation "resistant" or very far advanced, the marked palliative effect was considered as a notable accomplishment. In lymphosarcoma or reticulum cell sarcoma the results have not been so promising, but the authors cite several instances from the literature in which the outcome was more favorable. In chronic myelogenous leukemia and the asymptomatic stage of chronic lymphatic leukemia the effectiveness of HN_2 was often quite impressive. In the acute leukemias only very temporary alterations were obtained. The other malignant neoplasms treated likewise exhibited indefinite response. Ultimately, nitrogen mustard therapy proved ineffective in all lesions.

According to Wintrobe and Huguley, there are two disadvantages connected with the clinical application of the mustard therapy: (1) the nausea and vomiting which nearly always follows the first injection of each course, and (2) the depressant effect on the cellular elements of the blood resulting in lymphocytopenia, granulocytopenia, thrombocytopenia and some anemia. However, in the cases responding favorably this latter effect is short-lived and does not produce serious symptoms.

To eliminate some of these disadvantages Burchenal[8] tried the use of a new type of nitrogen mustard: the so-called Sk_{136} (1:3 propane diamine NNN'N' tetrakis (2-chloroethyl) dihydrochloride). Eleven patients with chronic myelogenous leukemia were treated with this drug. In general, Sk_{136}, when given in a dosage of 0.1 mg. per kilogram of body weight daily for four to eight doses, was found to cause much less nausea and vomiting than HN_2 but otherwise there was no difference in the clinical response. In 19 patients with acute leukemia SK_{136} remained largely unsatisfactory.

The question arose from the beginning of the clinical use of nitrogen mustard therapy whether or not its simultaneous applica-

[7] Wintrobe, M. M., and Huguley, C. M., Jr., Nitrogen mustard therapy for Hodgkin's disease, lymphosarcoma, the leukemias, and other disorders. *Cancer*, 1948, *1*, 357–382.

[8] Burchenal, J. H. The newer nitrogen mustards in the treatment of leukemia. *Radiology*, 1948, *50*, 494–499.

tion with roentgen therapy or other forms of irradiation may not be of advantage. Karnofsky, Burchenal, Ormsbee, Cornman and Rhoads[9] studied the additive toxicological effects of HN_2 and roentgen rays experimentally in mice. These experiments suggested that under certain conditions the destructive action of the two agents is at least additive. The impression was gained that the administration of a full course of HN_2 must precede the roentgen therapy to secure the best result. However, the authors emphasized that explorations of a much wider range are necessary before any definite recommendations can be made on this problem.

Since then several reports have appeared in the literature referring to various combinations of nitrogen mustard and roentgen therapy. In view of the clinical vagaries of the diseases for which the method is used and the very indefinite duration of the remissions that follow the treatment, however, it is still impossible to properly evaluate the cumulative effect of the two agents.

Their relative merit is much better understood. Craver,[10] on the basis of over 300 cases treated at Memorial Hospital and after reviewing the literature, summed this up as follows: (1) nitrogen mustard therapy is indispensable in (a) cases of generalized Hodgkin's disease with marked constitutional symptoms; (b) advanced cases of lymphosarcoma in which there is an immediate threat to life and in which the lesion causing the immediate danger is not amenable to surgery or irradiation; (c) anaplastic carcinoma of the lung; (2) in early and intermediate stages of Hodgkin's disease, in most cases of lymphosarcoma and in the majority of the chronic leukemias it seems doubtful that nitrogen mustard therapy offers any advantage or is as good an all around agent as roentgen therapy; and (3) none of the nitrogen mustards so far used has given any indication of ability to cure any of the types of cancer treated.

It may be said, as a general conclusion, that nitrogen mustard therapy has a marked palliative value. It undoubtedly will form an important adjunct of our future armamentarium in the treatment of certain well selected lesions. The trial of new compounds and the extension of the field of clinical exploration seems amply justified.

T. Leucutia, M.D.

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[9] Karnofsky, D. A., Burchenal, J. H., Ormsbee, R. A., Cornman, I., and Rhoads, C. P. Experimental observations in the use of the nitrogen mustards in the treatment of neoplastic disease. Approaches to Tumor Chemotherapy. Am. Assoc. Advancement Sc., 1947, pp. 293–305.

[10] Craver, L. F. The nitrogen mustards: clinical use. *Radiology*, 1948, *50*, 486–493.



ELDWIN R. WITWER
1890-1948

IN THE death of Dr. Eldwin R. Witwer, which occurred from a cerebral hemorrhage on November 2, 1948, the medical profession lost one of its abler physicians and radiology lost one of its staunchest champions in the fight to prevent encroachment on its rights and privileges as a speciality. His position in regard to issues of ethics, high scientific standards and economic justice was never in doubt, and his decided views were influential on the floor of scientific meetings as well as in private counsel and committee sessions.

Dr. Witwer was born in Ontario, Canada,

on August 23, 1890, but was educated in Michigan schools, Valparaiso University and the Detroit College of Medicine, now Wayne University College of Medicine. His earlier interests were in pathology and internal medicine and he held the position of Assistant Professor of Pathology in his Alma Mater, where he later became Assistant Professor of Radiology. For many years he was medical assistant to Dr. C. G. Jennings, an internist of national repute, and his excellent training in pathology and internal medicine was of course the finest possible basis for diagnostic and therapeutic radiology.

After a year of special study in the Department of Radiology at Cook County Hospital, Chicago, Dr. Witwer became radiologist to Jennings Hospital in Detroit and in 1927 he became associated with Drs. William A. Evans and Lawrence Reynolds, joining the staff at Harper Hospital. Although his major professional career was as radiologist to Harper Hospital, he also served in similar capacity on the staffs of Cottage, Bon Secours, U. S. Marine and Children's Hospitals.

His militant crusading spirit kept him in the vanguard of medical organizational activities. He was prominent in the conduct of the affairs of the local and state medical societies and had much to do with the policies of establishing and conducting the Michigan Medical and Hospital Services under the Blue Cross plan, serving as trustee of that organization. Because of his talent and willingness to work he was the perennial secretary of the Detroit Roentgen Ray and Radium Society, holding this position for twenty-two years, interrupted only by the time which he served as its president. The Radiological Society of North America honored him with its presidency for the year of 1945–1946. The American Roentgen Ray Society, the American College of Radiology, of which he was chancellor, and the American Medical Association all made use of his knowledge and industry in appointment to important committees. He was admitted to membership in the American Roentgen Ray Society in 1928 and was among the group certified as radiologists by the American Board of Radiology in 1934. The Rocky Mountain Radiological Society and the Indiana State Medical Society elected him to honorary membership.

Much could be written about Dr. Witwer's extra-medical activities, for they were many. An enthusiastic farmer, he belonged to a number of farm clubs and he was owner and breeder of fine blooded stock. An active Mason, he belonged to several masonic orders and was president of the Detroit Masonic Temple Association. His friends and acquaintances were legion and included farmers, tradesmen and laborers as well as captains of industry, and leaders in the professional world. He is survived by his wife, Maude Gibbing Witwer, and a daughter, Mary Ellen Witwer.

E. Walter Hall, M.D.

JOSÉ FRANCISCO MERLO GÓMEZ

WORD has come of the death on September 28, 1948 of Dr. José Francisco Merlo Gómez, one of the leading radiologists in South America. Dr. José F. Merlo Gómez was for many years an active member of the military establishment of the Argentine and Professor of Radiology in the Military Medical School. He graduated from the Faculty of the Medical School in Buenos Aires in 1912. He took post-graduate work in Europe, part of the time in Paris as an externe during the first world war. He served as assistant, then as head of the service in radiology in the Hospital de la Pitié.

In Argentina he served as chief of the x-ray service of the Surgical Clinic in the Hospital Nacional de Clinicas, as well as in a private sanitarium.

Dr. Merlo Gómez was President of the First Inter-American Congress of Radiology in Buenos Aires in 1943, and Honorary President of the Second Inter-American Congress of Radiology held in Havana in 1946.

Dr. Merlo Gómez was also a corresponding member of the Academy of Medicine of Colombia; honorary member of the American College of Radiology; Honorary President of the Inter-American College of Radiology, which he was chiefly instrumental in organizing; honorary member of the Cuban, Mexican, Colombian, and Peruvian radiological societies, and President of the Argentinian Society of Radiology.

Many of us here in the United States will recall with pleasure the visit of Dr. Merlo Gómez and his delightful family following the Havana meeting in 1946, and share the sorrow of Señora Gómez and their children.

JAMES T. CASE, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

AMERICAN RADIUM SOCIETY
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1949, to be announced.

AMERICAN COLLEGE OF RADIOLOGY
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: Atlantic City, N. J., June 8–10, 1949.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Next meeting time and place of Alabama State Medical Association,

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. A. H. Levy, 1354 Carroll St., Brooklyn 13, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. George L. Sackett, 10515 Carnegie Ave. Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday of October and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

HOUSTON X-RAY CLUB
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA X-RAY CLUB
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Moris Horwitz, 441 No. Camden Drive, Beverly Hills, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

LOUISVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August. Next meeting Sept. 27, 1948.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Robert M. Lowman, Grace-New Haven Community Hospital, New Haven 11. Meets bimonthly second Thursday, at place selected by Secretary.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting Jan. 7–8, 1949, Fort Worth, Texas.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. Ivan J. Miller, 49 Fourth St., San Francisco 3. Meets monthly on third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Langley Porter Clinic, University of California Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Roentgen Society
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 2100 Marlowe Ave., Montreal 28, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," *Villalta, 218, Lima.*

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

THE EASTERN CONFERENCE OF RADIOLOGISTS

The Eastern Conference of Radiologists is to be revived in the Spring of 1949. The Conference, previously known as the Mid-winter Conference of Eastern Radiologists, was suspended in 1940 due to World War II. Five cities participate, namely, Boston, New York, Philadelphia, Baltimore and Washington and it was the unanimous recommendation of the radiological societies in the respective cities that the Eastern Conference be revived. Washington, D. C., is to be the host city for a meeting on Friday and Saturday, March 11 and 12, 1949, with headquarters at the Hotel Statler. All radiologists are invited.

On the *pink insert* in the advertising section will be found detailed information concerning the meeting, with a registration form on the reverse side of the page. Those in charge of arrangements wish to gain an idea of the possible attendance at the meeting and they will appreciate having this registration form made out and sent in as soon as possible by those who plan to attend the meeting.

Below is given the detailed scientific program which has been arranged for the meeting of the Eastern Conference of Radiologists.

Friday Morning, March 11, 1949

Presidential Ballroom, Hotel Statler

9:00–10:15 A.M. PANEL DISCUSSION

The Correlation of Electro-Encephalography, Pneumo-Encephalography and Arteriography in the Diagnosis of Lesions of the Brain.

1. Roentgenological Aspects—George M. Wyatt, M.D., Moderator
2. Neurosurgical Aspects—Arthur A. Morris, M.D., Neurosurgeon, Doctors Hospital.
3. Neurological Aspects—Robert H. Groh, M.D., Associate in Neurology, Department of Neurology and Psychiatry, George Washington University Medical School.
4. Neuropathological Aspects—Webb Haymaker, M.D., Chief of Neurological Pathology Section, Army Institute of Pathology.

10:15–10:30 A.M. Intermission

10:30–10:45 A.M.

Supervoltage Radiation Therapy of Brain Tumors. Major Keene M. Wallace, M.C., Chief of Radiation Therapy, Walter Reed General Hospital.

10:45–11:00 A.M.

Congenital Vascular Anomalies (Phlebectasia). Captain Acors W. Thompson, M.C., Chief of Peripheral Vascular Section, Walter Reed General Hospital.

11:00–11:15 A.M.

Diagnostic Problems in the Normal and Pathological Physiology of the Colon. Dr. Willy E. Baensch, Professor of Roentgenology, Georgetown University Medical School and Hospital.

11:15–11:30 A.M.

Radiologist's Role in the Prevention and Early Diagnosis of Cancer of the Colon. Fred O. Coe, M.D., Radiologist. From the Radiological Clinic of Drs. Groover, Christie and Merritt.

11:30–11:45 A.M.

Differential Diagnosis of Inflammatory, Benign and Malignant Extrinsic Lesions of the Gastrointestinal Tract. Henry W. Wood, M.D., Fellow in Radiology. From the Radiological Clinic of Drs. Groover, Christie and Merritt.

Discussed by: Aubrey O. Hampton, M.D., Chief Radiologist, Garfield Memorial Hospital.

11:45–12:00 A.M.

Colon and Small Bowel Injury Following 1000 kv Roentgen Therapy. Colonel Harold I. Amory, M.C., Chief Radiologist, and Irving D. Brick, M.D., Consultant in Gastroenterology, Walter Reed General Hospital.

12:00–12:15 P.M.

A New Technique for Radium Therapy in Carcinoma of the Bladder. Milton Friedman, M.D., Consultant in Radiation Therapy, Walter Reed General Hospital, and Lloyd G. Lewis, M.D., Professor of Urology, Georgetown University Medical School.

12:15–12:30 P.M.

Primary Ureteral Tumor; a Case Report. William M. Clopton, M.D., Radiologist, *Sibley Memorial Hospital.*

12:30–2:30 P.M. Luncheon Period.

Friday Afternoon, March 11, 1949

National Bureau of Standards and The National Cancer Institute, United States Public Health Service

This part of the program will be held at the National Bureau of Standards. Buses from the Statler Hotel to the Bureau will be provided.

2:30–4:30 P.M.

Biological Effects of Chronic Irradiation with Gamma Rays on Laboratory Animals. By the Staff of the National Cancer Institute.

1. Introductory Remarks (5 min.). Egon Lorenz, Ph.D.
2. Effects on Breeding Behavior of Mice (20 min.). Margaret K. Derringer, Ph.D.
3. Pathology of Radiation Injury (20 min.). Allen B. Eschenbrenner, Ph.D.
4. Effects on Life Span, Hematopoiesis and Carcinogenesis (20 min.). Egon Lorenz, Ph.D.

Physical Aspects of X-ray Protection and Dosage Measurement. By the Staff of the National Bureau of Standards.

5. Conditions for the Economical Achievement of X-radiation Protection (20 min.). Harold O. Wyckoff, Ph.D.
6. Calibration Use of Thimble Chambers up to 1,400 kv. (20 min.). Lauriston S. Taylor, Ph.D.
7. Conditions for the Proper Utilization of Dosage Meters, Particularly in the Low Energy Range (20 min.). Frank H. Day, M.S.
8. Inspection of the Bureau of Standards' two new high voltage radiation laboratories.

Following the presentation of the papers the X-ray Section will hold an "open house" in its recently completed 1,400 kilovolt x-ray laboratory. In this will be shown the 1,400 kv. x-ray generator, x-ray tube, ion tube and electron tube, together with the special high pressure ionization chambers used with them. There will also be included the standardization laboratory for calibrating thimble chambers up to 200 kilovolts and for low voltage high intensity radiations such as obtained from contact therapy and beryllium-window tubes. The new multimillion-volt betatron laboratory will also be open for inspection. There are numerous other laboratories about the Bureau working on problems of direct or indirect interest to the radiologist.

6:30–8:00 P.M. Cocktails, Congressional Ballroom

8:00 P.M. Banquet, Presidential Ballroom

Saturday, March 12, 1948

Congressional Ballroom, Hotel Statler

9:00–10:15 A.M. PANEL DISCUSSION

The Management of "Surgically Incurable" Cancer of the Breast; a discussion devoted to the following specific aspects of the disease:

1. Local Lesions
2. Regional Nodes
3. Visceral Metastasis
4. Osseous Metastasis

Ralph M. Caulk, M.D., Moderator, Chief of Radiation Therapy, Garfield Memorial Hospital.

1. Surgical Aspects—Calvin T. Klopp, M.D., Medical Director, Warwick Memorial Clinic.
2. Radiation Therapy—U. V. Wilcox, M.D., Radiation Therapist, Doctors Hospital.
3. Endocrine Aspects—Roy Hertz, M.D., Chairman Endocrinology Section, National Cancer Institute; Associate, Warwick Memorial Clinic.
4. Neurosurgical Aspects—James W. Watts, M.D., Associate Professor of Neurosurgery, George Washington University Medical School.

10:30–10:45 A.M.

Tissue Distribution of some Organic Compounds of Radioisotopes. Charles F. Geschickter, M.D., Professor of Pathology, Georgetown University Medical School and Hospital.

10:45–11:00 A.M.

Prenatal Bowing of Tubular Bones; a Presentation of Cases. Francis C. Allman, M.D., Associate Radiologist, Providence Hospital.

11:00–11:15 A.M.

Orbital Foreign Bodies; Criteria for Detection and Discussion of the Pfeiffer Method for Precise Localization. Alfred A. J. Den, M.D., Radiologist, Episcopal Eye, Ear and Throat Hospital.

11:15–11:30 A.M.

Epilation in Ringworm of the Scalp (Microsporum auidini). Isidore Lattman, M.D., Radiologist, Children's Hospital.

11:30–11:45 A.M.

Intussusception; Reduced by Barium Enema (Hydrostatic Pressure). Isidore Lattman, M.D., Radiologist, and Gerald H. McAteer, M.D., Attending Surgeon, Children's Hospital.

11:45–12:00 A.M.

An Analysis of Approximately 7,000 "Positive" Chest Roentgenograms Encountered in a Recent Survey in the District of Columbia. Rollin F. Bunch, M.D., Fellow in Radiology. From the Radiological Clinic of Drs. Groover, Christie and Merritt.

Discussed by: Aubrey O. Hampton, M.D., Chief Radiologist, Garfield Memorial Hospital.

12:00–12:15 P.M.

Value of Chest Roentgenograms as a Routine Part of Cancer Detection Examinations. C. H. Wallman, M.D., Fellow in Radiology. From the Radiological Clinic of Drs. Groover, Christie and Merritt.

Discussed by: Aubrey O. Hampton, M.D., Chief Radiologist, Garfield Memorial Hospital.

12:15–12:30 P.M.

The Clinical Application of Radioisotopes in the Diagnosis and Treatment of Cancer. Murray M. Copeland, M.D., Professor of Oncology and Radiotherapist, Georgetown University Hospital.

12:30–12:45 P.M.

Results of Radiation Therapy alone in Adenocarcinoma of the Uterine Cervix and Corpus. George D. Adams, M.D., Fellow in Radiology. From the Radiological Clinic of Drs. Groover, Christie, and Merritt.

THIRD INTER-AMERICAN CONGRESS OF RADIOLOGY

The Third Inter-American Congress of Radiology will be held in Santiago, Chile, from November 11 to November 17, 1949. Prior announcements of the meeting (see especially this Journal, page 559, October, 1948) have elicited many inquiries requesting information regarding transportation to and from Santiago.

The radiologist who has ample time and would enjoy an ocean voyage can sail from New York or New Orleans and arrive in Rio de Janeiro twelve days later. A program of visits to medical institutions and scenic high spots can be arranged in Rio; thence to Sao Paulo, via Pan American World Airways, visiting Montevideo, Buenos Aires, the Chilean lakes district, and Santiago.

After the Congress has ended, a northern flight can be arranged with stops at Arequipa, the Incaland Country, Lima, Quito, Cali, Bogota, Medellin, Balboa, C. Z., Guatemala, Merida, Yucatan, Mexico, and finally New Orleans.

Physicians who are pressed for time but who would like to attend the Santiago meeting may fly directly from New York, New Orleans, Miami, or Mexico City, to Santiago.

Special itineraries will be made for those who wish to attend the Congress, and will be personalized to include such stops as are chosen.

Dr. James T. Case, 55 East Washington Street, Chicago 2, Illinois, chairman of the Committee on International Affairs of the American College of Radiology, will be happy to assist all interested radiologists in making their plans. Because of the great demand for South American transportation during the winter months, all those who foresee a possibility of attending the Third Inter-American Congress of Radiology should write Doctor Case immediately.

THE AMERICAN BOARD OF RADIOLOGY

Certification of Radiation Physicists

Beginning January 1, 1949, The American Board of Radiology will examine and certify physicists as radiation physicists. Three types of certificates will be granted:

(1) Radiological Physics
(2) X-ray and Radium Physics
(3) Medical Nuclear Physics

(2) and (3) are both included in (1).

Each applicant for any one of the certificates in radiation physics will be required to meet the following standards:

(a) Satisfactory moral and ethical standing.

(b) That he holds himself to be a specialist in the category of physics designated in his application.

(c) That he be a citizen of the United States or Canada. Candidates from other countries must be permanent residents of that country and native citizens thereof.

(d) That he holds a degree of Bachelor of Arts or its equivalent and has majored in physical science or engineering.

(e) That he be a member of the American Physical Society or similar organization.

(f) That after graduation from college he has had at least one year postgraduate experience in radiation physics or in a radiation physics laboratory.

(g) Candidates for examination in Radiological Physics in addition to requirements specified in paragraphs (a), (b), (c), (d), (e) and (f) must have had at least one year of experience in association with a Department of Radiology approved by the Board and throughout one of the two years specified must have had experience in medical application of artificial radioactive materials.

Each candidate shall submit with his application personal records of calibrations of one low voltage and one high voltage x-ray apparatus, personal records of one x-ray protection survey and one protection survey for radioactive materials.

(h) Candidates for examination in X-ray and Radium Physics in addition to requirements specified in paragraphs (a), (b), (c), (d), (e) and (f) must have had at least one year of experience in association with a Department of Radiology approved by the Board. With the application he must submit records of personal calibration of one low voltage and one high voltage x-ray apparatus and personal records of one x-ray protection survey and one personal protection survey for radium.

(i) Candidates for examination in Medical Nuclear Physics in addition to requirements specified in paragraphs (a), (b), (c), (d), (e) and (f) must have had one year of experience in physical procedures relative to medical application of radioactive materials.

(j) Applications shall be endorsed by a Diplomate of the American Board of Radiology and a Diplomate in Radiological Physics who have personal knowledge of the experience, training, moral and ethical standing of the applicant and that he is qualified to take an examination.

(k) A fee of $25.00 shall accompany the application which will be refunded if the application for examination is not accepted.

(l) Applications shall be submitted to the Secretary of The American Board of Radiology. He shall forward them to the Credentials Committee on Radiological Physics to be appointed by the Board, who shall decide about the candidate's fitness to be examined. Those approved for examination shall be informed by the Secretary of the Board when and where to appear.

Examinations will usually be conducted at the time and place of the regular or special meetings of the American Board of Radiology.

Examinations in radiation physics shall be oral though practical or written examinations may be required. Examinations will be designed to test the candidate's knowledge and his fitness to practice physics in the category for which he applies. Accordingly, the examination may include questions regarding the structure of matter, construction and operation of x-ray apparatus, the use of radiation measuring instruments, determination of radiation quantity and quality, protection from x-rays, radium and artificial radioactive substances, preparation of radioactive applicators, determination of dosages of x-rays, radium and radioactive substances and other questions relative to the category in which the candidate applies.

Candidates who fail an examination shall not be admitted to another examination until one year has elapsed. They must request re-examination at least sixty days prior to the next meeting of the Board and pay an additional fee of $10.00.

A diploma may be revoked if in the opinion of the Board a misstatement of fact has been made in the application or any other communication to the Board or its representatives, or for expulsion from a scientific society for misconduct. Under such circumstances the diplomas must be returned to the Board and the name of the individual shall be omitted from the Registry of Diplomates.

Address all communications to the Secretary of the American Board of Radiology.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

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INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Neck and Chest

DOCK, W.: Reasons for the common anatomic location of pulmonary tuberculosis..... 119
DOIG, A. T., and MCLAUGHLIN, A. I. G.: Clearing of x-ray shadows in welders' siderosis.. 119
WEARING, J. D. H.: Bronchiectasis simulating chronic bronchitis..... 120
NORRIS, C. M.: Early clinical features of bronchogenic carcinoma..... 120
HERBUT, P. A., and CLERF, L. H.: Cancer cells in bronchial secretions..... 120
BLAIR, L. G.: Interpretation of children's chest x-rays..... 121
STEPHENS, H. B.: Congenital pulmonary stenosis..... 122
HUGHES, F. A., JR., and WESTPHAL, K. F.: Amebiasis with pulmonary involvement..... 122
GROSS, R. E.: Surgical treatment for coarctation of the aorta..... 123
LONGMIRE, W. P., JR.: Congenital atresia and tracheoesophageal fistula..... 123
GUY, C. C., and OLECK, H. T.: Traumatic biliary-bronchial fistula..... 123

Abdomen

RITVO, M., and SCHAUFFER, I. A.: Roentgenographic studies of gastro-intestinal tract following section of the vagus nerves for peptic ulcer..... 124
PEIN, N. K.: Neonatal gastrocolic fistula..... 124
FALLE, E. DE C.: Pyloric spasm simulating congenital hypertrophic stenosis..... 124
TAYLOR, H.: Carcinoma of the stomach..... 124
KANE, F. F.: Acute intestinal obstruction in typhoid fever..... 125
HANSEN, P. S.: Hemangioma of the small intestine..... 125
COLVERT, J. R.: Rectal polyps..... 125
HARRINGTON, S. W.: Various types of diaphragmatic hernia treated surgically..... 126
MEYER, K. A., ROSI, P. A., and STEIN, I. F.: Studies on vagotomy in the treatment of peptic ulcer. II. Clinical evaluation..... 126
STEIN, I. F., and MEYER, K. A.: Studies on vagotomy in the treatment of peptic ulcer III. Physiological aspect..... 127
BERG, B. N.: Gastric ulcers produced experimentally by vascular ligation..... 127
FERRER, J. M., JR.: Effect of tetra-ethyl ammonium chloride on gastric secretion and acidity in peptic ulcer..... 127
METZ, A. R.: Duodenal regurgitation..... 127
HEIFETZ, C. J., and SENTURIA, H. R.: Acute pneumocholecystitis..... 128
KITTLE, C. F., JENKINS, H. P., and DRAGSTEDT, L. R.: Patent omphalomesenteric duct and its relation to the diverticulum of Meckel..... 128
BENEVENTI, F. A., and TWINEM, F. P.: Neuroblastoma..... 129
MILLER, E.: Malrotation of the colon..... 130
POTTS, W. J.: Congenital atresia of intestine and colon..... 130
SARNOFF, S. J., ARROWOOD, JULIA G., and CHAPMAN, W. P.: Differential spinal block..... 130
LEITHAUSER, D. J.: Atypical adynamic ileus apparently caused by nutritional (thiamine chloride) deficiency..... 131

Genitourinary System

ANTOPOL, W., and GOLDMAN, L.: Subepithelial hemorrhage of renal pelvis simulating neoplasm..... 131
HALE, N. G.: Primary papillary carcinoma of the ureter..... 132
MELICK, W. F., and VITT, A. E.: Present status of aortography..... 132
EDELSTEIN, J. M., and MARCUS, S. M.: Primary benign neoplasm of the ureter.... 133
CAMPBELL, M. F.: Congenital hydronephrosis and hydroureter..... 133
MCGAVRAN, H. G.: Giant prostate without symptoms: neurofibroma..... 133
BEATTY, R. P.: Life expectancy in carcinoma of prostate..... 134

Skeletal System

HAUSER, E. D. W., and CONSTANT, G. A.: Skeletal hemangio-endothelioma..... 134
FAIRBANK, H. A. T.: Osteopetrosis..... 134
FEJER, E.: Interesting case of melorheostosis..... 135
ALDERSON, B. R.: Further observations on fracture of the first rib..... 135

BRAILSFORD, J. F.: Some experiences with bone tumours 136
SHACKMAN, R., and HARRISON, C. V.: Occult bone metastases 137
HITCHCOCK, H. H., and BECHTOL, C. O.: Painful shoulder 137
DAVIES, H.: Unstable semilunar bone 137
IMMERMANN, E. W.: Dislocation of the pisiform 137
ANDREASEN, A. T.: Congenital absence of humeral head 138
McDONNELL, D. P., and WILSON, J. C.: Fractures of lower end of humerus in children 138
ANDREASEN, A. T.: Avulsion fracture of lesser tuberosity of humerus 139
SHELLITO, J. G., and DOCKERTY, M. B.: Cartilaginous tumors of the hand 139
UMANSKY, A. L., SCHLESINGER, P. T., and GREENBERG, B. B.: Tuberculous dactylitis in the adult 140
BERK, M. E.: Gout 140
BURROWS, H. J.: Fatigue fractures of the fibula 141
ROLLESTON, G. L.: Early radiological diagnosis of ankylosing spondylitis 141
BARNES, R.: Paraplegia in cervical spine injuries 142
TAYLOR, A. R., and BLACKWOOD, W.: Paraplegia in hyperextension cervical injuries with normal radiographic appearances ... 142
KRISTOFF, F. V., and ODOM, G. L.: Ruptured intervertebral disk in cervical region 143
PEYTON, W. T., and SIMMONS, D. R.: Herniated intervertebral disk 143
CLEVELAND, M., BOSWORTH, D. M., and THOMPSON, F. R.: Pseudarthrosis in lumbosacral spine 144
HORWITZ, T.: Treatment of congenital (or developmental) coxa vara 144
BOST, F. C., HAGEY, HELEN, SCHOTTSTAEDT, E. R., and LARSEN, L. J.: Results of treatment of congenital dislocation of hip in infancy 145
DONALDSON, S. W., BADGLEY, C. E., and HUNSBERBER, W. G.: Lateral view of pelvis in examination for hip dislocation 146

ROENTGEN DIAGNOSIS

NECK AND CHEST

DOCK, WILLIAM. Reasons for the common anatomic location of pulmonary tuberculosis. *Radiology*, April, 1947, *48*, 319–322.

As the cardiac output is less when the subject is sitting or standing than in recumbency, and pulmonary arterial pressure varies with the output, even lower pressure must occur in the right ventricles of persons who sit or move but little while on their feet. This means that the column of blood from the right heart to the apical part of the lungs exerts an equal or greater pressure. In view of the fall in pressure along the course of the vessel, there can scarcely be any blood flow, and no formation of lymph or tissue fluid at the upper third of the lungs under these conditions. Because of the length and tortuosity of the right pulmonary artery pressure on that side will be lower and the bloodless region larger than on the left.

As is well known primary lung lesions initiated prior to development of resistance are disseminated generally throughout the lungs of men, cattle, and rabbits. It seems probable that in animals or men with reinfection or with rapid development of high resistance an inadequate pulmonary blood flow, for many hours each day, may permit tuberculosis to progress in the lung field highest above the heart, while lower parts enjoy a considerable degree of immunity. In adults, progressive lesions observed soon after reversal of a negative skin test are usually in the upper lung field, and in the usual instances of "reinfection," apical disease progresses and the opposite apex becomes involved even though other regions, in spite of a constantly positive sputum, remain free for months, years, or decades.

One reason for accepting the probability that relative ischemia is the basis for the apical location of phthisis in man is the very low incidence of progressive apical lesions in patients with mitral stenosis and the very high incidence in those with pulmonic stenosis.

The significance of this theory, in treatment by bed rest and collapse is that absolute recumbency, not rest in the propped up or sitting posture, is the factor most important in management.—*James J. McCort, M. D.*

DOIG, A. T., and McLAUGHLIN, A. I. G. Clearing of x-ray shadows in welders' siderosis. *Lancet*, May 22, 1948, *1*, 789–791.

This is a follow-up study of the authors' original (1936) description of a siderosis due to inhalation of nearly pure iron oxide particles

in welding fumes. At that time they concluded that the opacity noted in roentgenograms might be due to the iron oxide alone, without the association of fibrosis and congestion. The confirmatory literature since that time is quoted, including the only case of a postmortem examination in a previously known welders' siderosis. No fibrosis was found in the lung tissue.

The present follow-up includes one man who quit welding because of his abnormal chest film. Follow-up films were unchanged for two years. The patient was lost track of until nine years after he was first seen. At this time there was complete clearing of the previously described siderosis.

A second man became an instructor of welding. At this occupation only one-fourth of his time was spent at active welding. His chest film showed considerable resolution of the original process.

These 2 cases provide evidence that the roentgenographic reticulation and nodulation of welders' siderosis is not necessarily permanent, and that iron oxide dust can be eliminated from the lung parenchyma after some years.—*J. S. Summers, M. D.*

WEARING, J. D. H. Bronchiectasis simulating chronic bronchitis; a study of 46 cases. *Lancet*, May 29, 1948, *1*, 822–824.

There is a large group of patients with bronchiectasis in whom the symptoms and physical signs closely resemble chronic bronchitis. During a period of eighteen months at a military hospital the author examined 211 men and 3 women with signs of a chronic bronchitis, but without signs and symptoms classically attributed to bronchiectasis. Bronchograms of each patient revealed 46 (21 per cent) to have bronchiectasis. There were 31 cases of cylindrical, 3 of varicose and 12 of saccular type bronchiectasis.

In 26 (56 per cent) of the patients with bronchiectasis there was a history of "pneumonia." In the 168 cases without bronchiectasis only 32 per cent gave a history of "pneumonia." The author believes that the bronchi in unresolved pneumonia at first undergo reversible mechanical dilatation which may later be rendered irreversible by secondary infection of the bronchial wall. A bronchus may remain dilated for several months and yet be capable of returning to its original diameter.

In certain forms of bronchiectasis, a plain film is difficult to interpret correctly. Only by bronchography is accurate diagnosis of bronchiectasis possible in the living subject.—*J. S. Summers, M.D.*

NORRIS, CHAS. M. Early clinical features of bronchogenic carcinoma; illustrative cases. *Dis. of Chest*, March-April, 1948, *14*, 198–217.

Analysis of 310 proved cases of bronchogenic carcinoma seen at Chevalier Jackson Bronchoscopic Clinic shows a histological diagnosis was made during life in 97 per cent, of which bronchoscopic biopsy yielded 71 per cent and aspiration biopsy 14.5 per cent. Early manifestations of bronchial carcinoma depend on the point of origin of the lesion. About 50 per cent arise in the main stem, or lobar bronchus; about 25 per cent each rise in the segmental bronchi, and peripheral branches. The author describes the clinical symptoms and physical findings correlating them with case reports and films of the origin of the tumor. The main bronchus lesion may give no positive roentgen findings, but in this series, only 6 of 310 chest films were thought to be essentially negative. The author stresses the value of bronchoscopy when symptoms persist and films are negative. The secondary effects of tumor are described such as bronchial obstruction with atelectasis or ball-valve emphysema, which is seen on fluoroscopy. Segmental bronchial tumors usually show a wedge-shaped atelectasis. The peripheral tumors are frequently "silent" and may not be discovered until considerable size gives rise to pulmonary symptoms. Aspiration biopsy in 69 cases gave a positive diagnosis of malignancy in 45, or 66 per cent.—*Fred R. Gilmore, M.D.*

HERBUT, PETER A., and CLERF, LOUIS H. Cancer cells in bronchial secretions. *Tuberculology*, Dec., 1947, *9*, 90–92.

The authors outline the method of examination of bronchial secretions obtained by the bronchoscope in an attempt to make an earlier diagnosis of lung carcinoma. Using the Papanicolaou technique they examined 525 preparations of which 118 cases are proved carcinoma; cancerous cells were present in 105 cases, or 89 per cent, while a positive bronchoscopic biopsy was made in 52 cases, or 44 per cent. However, in 32 cases, or 27 per cent, the bronchoscopic examination was completely negative, but neoplastic cells were found in the bronchial secretions. There are three types of

tumor cells classified: squamous, completely undifferentiated, and all others. The first group comprises cells in clumps or alone. These contain moderate cytoplasm with deeply staining pleomorphic nuclei; occasionally, there are typical pearls present. The undifferentiated group usually shows single cells with scanty cytoplasm and a round, deeply staining homogeneous nucleus. The last group varies widely. Nevertheless, when there are inflammatory or Langhans cells present, these do not imitate the neoplastic cells.—*Fred R. Gilmore, M.D.*

Blair, L. G. Interpretation of children's chest x rays. *Brit. J. Radiol.*, June, 1947, *20*, 223–237.

The first step in interpretation of the chest film of an infant is an assessment of the technical factors. If the child was rotated or if the exposure was made in some other phase than full inspiration, the heart and mediastinum are much broader and the lung markings are crowded, suggesting collapse; or there is generalized diminished translucency. If the exposure is made during rapid inspiration, part of the lung may actually appear consolidated. Films made in strenuous expiration with crying may show a mediastinum which is very wide and apparently grossly pathological. Exposures made supine with slight rotation show considerable displacement of the mediastinum, which, being very mobile, usually falls off the spine.

Although the pathological changes which occur in children's chests may be the same as those in adults, there is a large group of specifically infants' diseases which are to be kept in mind. Elevation of the whole of one diaphragm leaf might indicate increased intra-abdominal pressure, Petit's eventration, or subdiaphragmatic abscess. A portion of the diaphragm may be elevated because of localized muscle weakness with bulging in one area; liver cysts or abscesses produce a similar situation. Diaphragmatic hernia, congenitally short esophagus, or even absence of one leaf sometimes enter into the differential diagnosis and are to be considered.

The bony structures of the thorax reflect generalized bone diseases, and rickets and scurvy may be diagnosed in this manner. Xanthomatosis and bone tuberculosis are to be kept in mind in dealing with children. Bone destruction in the region of a tumor suggests an inflammatory process as the ribs in children give more readily than adult structures to pressure and a malignant tumor is more likely to displace the ribs than destroy them.

Fluoroscopy is important in demonstrating unusual shift of the mediastinum in bronchial obstruction. The mediastinum shifts toward collapse, consolidation, long-standing effusion, and also toward the side in which there is agenesis of a lobe or the lung. In the last instance there is emphysema on the side of the chest toward which the mediastinum shifts. Shift is away from a recent effusion and obstructive emphysema.

Enlargement of the mediastinum due to tuberculosis is indistinguishable from that due to Hodgkin's disease or lymphosarcoma. Other mediastinal enlargements are usually fairly easily differentiated. An enlarged thymus resembles a Phrygian cap superimposed upon the heart. A dermoid cyst is well anterior and rarely causes displacement of the esophagus or trachea. A paravertebral abscess is easily diagnosed if the possibility is remembered. It is posterior and associated with vertebral destruction. Dilatation of the esophagus due either to stricture or cardiospasm is easily diagnosed with barium but the possibility must be considered.

There are certain causes for increased translucency in lung:

1. Pneumothorax is easily identified, but tension pneumothorax is to be remembered as an important type which may call for intervention.

2. Generalized emphysema in children is usually associated with asthma. When localized it may be conpensatory to collapse or due to the ball valve action of a foreign body. Enlarged mediastinal glands may produce the same effect and the resultant emphysema may be the only indication of tuberculosis.

3. Cysts may be congenital or may result from inflammation such as bronchiectasis.

4. Cavities are seen in lung abscesses and are often indistinguishable from cavities seen in primary tuberculosis. The rare adult type of tuberculosis produces typical tuberculous cavities.

Opacities in the lungs may be divided into several groups:

1. Mottled opacities when localized are usually pneumonia; when generalized are usually miliary tuberculosis, either acute or chronic, though leukemia may produce a similar appearance. Carcinoma metastasizing to lung produces mottled opacities of varying size; in

sarcoma the lesions are usually larger and the appearance is typical.

2. Rounded opacities should be carefully identified as to whether they are pulmonary or pleural. In the lung the commonest cause is tuberculosis. Other causes are rarer, as hydatid cyst, congenital cyst, metastasis, or primary neoplasm. Thoracotomy is usually necessary for diagnosis. In the pleura the usual possibilities are neoplasm, fluid-containing cyst, or encysted effusion. The commonest tumors are those arising from the nervous tissue.

3. Non-rounded opacities in the pleura are almost always clear effusion or pus. Small ones are particularly difficult to recognize and are particularly important as they frequently accompany tuberculosis.

4. Segmental opacities in lung are the most common opacities and represent varying degrees of consolidating or collapse. They are due to inflammation, pressure from tuberculous gland on a bronchus, ulceration of the gland into the bronchus, an aspirated foreign body or primary neoplasm.

5. Linear opacities are accessory fissures, fibrosis, complete collapse of a small segment or bronchiectasis. Fibrosis is accompanied by displacement of mediastinal structures. Bronchiectasis may supervene after collapse due to primary tuberculosis.

An instructive series of roentgenograms accompanies this paper—*E. F. Lang, M.D.*

STEPHENS, H. BRODIE. Congenital pulmonary stenosis. (Editorial) *Surg., Gynec. & Obst.*, June, 1948, *86*, 758–760.

The most frequently encountered type of congenital cardiovascular defect accompanied by cyanosis is termed the tetralogy of Fallot (pulmonary stenosis, dextroposition of the aorta, interventricular septal defect and right ventricular hypertrophy). This malformation results in a greatly diminished flow of blood through the pulmonary artery. Cyanosis and clubbing of the fingers are due to the venous-arterial mixing that occurs through the interventricular septal defect where the flow is from right to left and venous blood from the right ventricle passes out into the overriding aorta directly into the systemic circulation.

Taussig emphasizes certain characteristic clinical findings that are helpful in establishing the diagnosis of the tetralogy of Fallot, to wit, the heart is normal in size, and usually a basal systolic murmur and pure second sound are audible. The electrocardiogram shows a right axis deviation. The roentgenogram demonstrates an absence of the normal fullness of the pulmonary conus and the lung fields are clear. Fluoroscopy shows no pulsations at the hilum of the lungs. There are, however, according to Taussig, many variables in these clinical findings.

Anastomosis of one of the major systemic arteries to the right or left pulmonary artery is often spoken of as the Blalock operation. Blalock and Taussig have advocated this operation to increase the pulmonary blood flow in that there is a definite lack of circulation to the lungs in congenital pulmonary stenosis. The great value of this operation has been demonstrated in several hundred cases that have been managed by Blalock and his associates.—*Mary Frances Vastine, M.D.*

HUGHES, FELIX, A., JR., and WESTPHAL, KEAN F. Amebiasis with pulmonary involvement. *Arch. Surg.*, Sept., 1947, *55*, 304–315.

The authors estimate that about 10 or 20 per cent of the population harbor *Endamoeba histolytica* and suggest that the percentage is at least twice as high in soldiers returning from overseas.

The incidence of hepatic involvement in cases with dysentery apparently varies from about 9 per cent in early well treated cases to 95 per cent in the fatal ones. Pleural and pulmonary complications have been described in 5 to 15 per cent of the patients with dysentery and from 10 to 20 per cent of those with hepatitis.

Once the liver has been involved, the pleura and lungs may become affected as the result of direct extension of the disease through the diaphragm. If the pleura alone is involved, a sterile empyema may develop. Bronchobiliary fistula without empyema or pneumonitis has been described. The most common process, however, is a diffuse pneumonitis of the right lower lobe associated with an abscess or a bronchopulmonary fistula.

The authors believe that amebic hepatopulmonary disease occurs often enough to be included in the differential diagnosis of diseases of the right upper abdominal quadrant or right lower portion of the chest. The diagnosis depends upon the finding of *Endamoeba histolytica* or by the specific response to emetine hydrochloride.

When the pleura becomes involved, cough and pain in the chest aggravated by deep

breathing and finally pleural effusion make their appearance. When the lungs become involved, the cough becomes productive of a bloody purulent sputum in which the organism may often be found.

According to the authors, the earliest roentgen manifestations of threatened bronchopulmonary involvement include elevation and fixation of the right hemidiaphragm plus some irregularity in its configuration. They describe a characteristic triangular shadow in the base of the right lung which extends from the hilum as its apex, to the liver. Bulging with obliteration of the cardiophrenic and anterior costophrenic angles are also described. The presence of a cavity in the lungs and the actual demonstration by means of a contrast substance of the bronchohepatic fistula have been demonstrated.

The records of 3 patients with amebic infections of the lung are reported and their roentgenograms reproduced.—*Philip J. Hodes, M.D.*

Gross, Robert E. Surgical treatment for coarctation of the aorta. (Editorial) *Surg., Gynec. & Obst.*, June, 1948, *86*, 756–758.

This anomaly is more common in men than women. In patients with coarctation who live past the first two years of life, certain generalities can be made. One of four eventualities may overtake him: (1) he may live a long life and have little or no important complaints related to the vascular obstruction; (2) he may die suddenly from aortic rupture. This fatal complication is most common in the third decade of life; (3) he may die from superimposed *Streptococcus viridans* infection, a complication which was most common during the second and third decades. Such a threat is less likely in the present day of chemotherapy; (4) he may die of the hypertensive state—from cardiac failure or from intracranial hemorrhage.

In a series of 40 patients with coarctation treated by the author, the following results were obtained: (These patients ranged in age from seven to thirty-one years.)

1. The thoracic duct was not injured in any case.

2. In 5 instances, only exploration was carried out; the operation was terminated because the narrowed segment of aorta was very long or else the vessels were surrounded by an inflammatory reaction as a result of previous infection.

3. In 35 cases the narrowed portion of aorta was excised and the remaining ends of the vessel were brought together.

4. There were 5 deaths in this last group.

5. Specimens removed from the 35 patients showed a complete block in 5 and in the remainder there was a tiny opening.

6. The optimum ages for procedures of this sort appear to lie between ten and twenty years. —*Mary Frances Vastine, M.D.*

Longmire, William P., Jr. Congenital atresia and tracheoesophageal fistula. *Arch. Surg.*, Sept., 1947, *55*, 330–338.

The author calls attention to the fact that the most important step in the treatment of these patients is the early recognition of the anomaly by the attending physician before the infant's life is seriously threatened by aspiration pneumonia, or dehydration, and starvation.

The success or failure of the operative procedure depends in large part on the general condition of the patient at the time of operation.

The author reports 4 consecutive patients with tracheoesophageal fistulas and esophageal atresia who survived ligation of the fistula and primary anastomosis of the esophagus. All of the patients are now taking feedings by mouth and are gaining weight satisfactorily.—*Philip J. Hodes, M.D.*

Guy, Chester C., and Oleck, Henry T. Traumatic biliary-bronchial fistula. *Arch. Surg.*, Sept., 1947, *55*, 316–329.

The authors call attention to the rather uncommon occurrence of biliary-bronchial fistulas in patients suffering combined thoraco-abdominal wounds. That this is not due to an excessive and early mortality rate is supported by the fact that 70 per cent of patients with abdominothoracic wounds on the right side survive and 50 per cent of the patients with similar wounds on the left side survive. The fact that wounds of the liver are usually either rapidly fatal from hemorrhage or else heal surprisingly well is generally recognized. Of considerable significance also is the fact that even though portal blood and liver commonly harbor pathogenic bacteria, there is no evidence that wounds of the liver show any particular tendency to become infected.

The authors postulate the presence of some interference with the free flow of bile in patients who develop biliary-bronchial fistulas. They also believe that in the presence of considerable

liver necrosis, abscess cavities may result which predisposes to biliary-bronchial fistulas. It is their opinion that the essential pathologic process begins in the liver and that effective surgical therapy must be directed primarily to the liver.—*Philip J. Hodes, M.D.*

ABDOMEN

RITVO, M., and SHAUFFER, I. A. Roentgenographic studies of the gastro-intestinal tract following section of the vagus nerves for peptic ulcer. *New England J. Med.*, April 8, 1948, *238*, 496–501.

Thirty-three patients with bilateral vagus resection for peptic ulcer were studied by film and fluoroscopic methods at the Boston City Hospital. Twenty-nine of the operations were supradiaphragmatic and 4 transabdominal. Thirty patients were male and 3 female. The ages ranged from twenty-one to fifty-seven. Twenty-one patients had no previous gastric surgery, 3 had had previous gastroenterostomies, and 5 had had partial gastrectomy followed by marginal or jejunal ulcer. Of the twenty-one patients without previous surgery, 20 had duodenal ulcers, and 1 had an ulcer on the lesser curvature of the stomach.

In the first weeks after operation, the stomach exhibited dilatation, atonicity and sluggish, ineffective peristalsis. Emptying time was markedly increased. After several months, all of these changes tended to return toward the normal, although one patient with very poor emptying required a subsequent gastroenterostomy. The duodenal bulb improved in caliber after operation. In patients with previous surgery, gastric dilatation and delay was less marked, and the stomal and jejunal ulcers healed promptly.

One patient developed temperature dysphagia after transabdominal vagus resection. Roentgen examination showed changes suggestive of cardiospasm, with narrowing of the lower end of the esophagus, reverse peristalsis and delay in esophageal emptying.—*Henry P. Brean, M.D.*

PEIN, N. K. Neonatal gastrocolic fistula; report of a case. *Lancet*, July 10, 1948, *2*, 53–54.

Report of one case in a five week old infant with greenish slimy undigested food per rectum and a fecal character to vomitus.

Diagnosis proved by roentgenography after a bismuth meal. The bismuth flowed directly from stomach into transverse colon. At operation the fistula appeared to be of inflammatory origin. The baby died two days after operation. At necropsy an ulcer 3 mm. in diameter was found inside the stomach. On section this appeared to be a small chronic gastric ulcer.

The author believes the findings strongly suggest a peptic ulcer which, starting in fetal life, had perforated the adjacent colon.—*J. S. Summers, M.D.*

FALLE, E. DE C. Pyloric spasm simulating congenital hypertrophic stenosis; report of a case. *Lancet*, May 22, 1948, *1*, 794.

A girl, aged six weeks, presented all the classical signs and symptoms of a typical pyloric stenosis and a roentgenographic picture of almost complete obstruction at the pylorus. After conservative medical regimen failed, an exploratory laparotomy revealed no organic pathology. After operation glyceryl trinitrate was used to relax the pylorus. Barium meal study showed a normal appearance.—*J. S. Summers, M.D.*

TAYLOR, H. Carcinoma of the stomach. *Lancet*, April 17, 1948, *1*, 581.

Each year 13,000 people in England die of carcinoma of the stomach. Only 70 per cent of these are seen in a hospital. Five out of 6 are beyond cure when they are first seen in the hospital. Of each 5 hopeless cases, 2 have clinically recognizable metastases on arrival, 1 is generally too ill for operation, and 2 are found to be inoperable on laparotomy. The 1 patient in 6 whose growth is removed submits his life to a 30 per cent risk. If he survives the crisis he has half the normal life expectancy.

The author deplores these facts, then suggests a plan whereby everyone in England under the new health service program and between the ages of forty and sixty-five (roughly 15,000,000 people) may have a barium meal study for even the most vague abdominal complaint. He suggests that if 1 in 25 of this age group had complaints, 50,000 barium meals would be needed each year. This need could be met by ten roentgen-ray units in each of the twelve health service regions, if each unit could do 20 studies a day. This is not an impossible goal.

He is appalled and depressed by the endless succession of hopeless laparotomies or desperate dissections of too extensive growths, and feels

that the proposed program, though not perfect, would increase the number of patients referred for treatment while still in the operable stage.—*J. S. Summers, M.D.*

Kane, F. F. Acute intestinal obstruction in typhoid fever. *Lancet*, July 17, 1948, *2*, 97–98.

This is a report of an unusual case of typhoid fever, admitted to the hospital sixteen hours after onset of symptoms because of history of ingestion of contaminated milk. Combined penicillin and sulfathiazole gave disappointing results. On the evening of the forty-third day after an acute abdominal pain, exploratory laparotomy revealed an acute intestinal obstruction caused by peritoneal bands, probably due to stretching of adhesions formed over areas of typhoid ulceration. Division of the bands relieved the abdominal symptoms, but death followed from typhoid septicemia.—*J. S. Summers, M.D.*

Hansen, Paul Scott. Hemangioma of the small intestine with special reference to intussusception; review of the literature and report of three cases. *Am. J. Clin. Path.*, Jan., 1948, *18*, 14–42.

Hemangiomas (Raiford) compose 6 per cent of benign tumors and 3.4 per cent of all tumors of the small intestine. Fifteen to 30 per cent of all benign tumors of the small intestine cause intussusception, but hemangiomas relatively rarely cause this condition (as will be noted according to the classification). Kaisjer's adaptation of Oberndorff's classification is as follows:

1. Multiple phlebectasia—multiple dilated venous structures, microscopically cavernous in type, grossly pin-head to pea-sized, purple nodules. Rarely cause symptoms.
2. Cavernous hemangioma.
 (a) Diffuse infiltrating cavernous hemangiomas; cavernous tissue usually invades all layers sparing mucosa and muscularis and results in narrowing of the lumen by thickening of the wall. Lesions are probably solitary. Hemorrhage occurs in most. Symptoms of obstruction in 50 per cent.
 (b) Circumscribed often polypoid, cavernous hemangioma. Always single and always cavernous. Not infrequently cause hemorrhage and, when polypoid, can cause intussusception.
3. Simple capillary hemangioma. Capillaries are not grossly dilated as in the foregoing type. Tumor is usually spherical and projects into the lumen and is frequently the size of a plum. Majority are found in the ileum. Hemorrhage, obstruction and intussusception are noted.
4. Hemangiomatosis localized in the gastrointestinal tract. A portion of the widespread hemangiomatosis involving particularly skin and liver. Relatively asymptomatic, with the exception of occasional hemorrhage, obstruction or intussusception.

Diagnosis of hemangioma of small bowel is rarely made preoperatively. Diagnosis is perhaps improved if the following are noted:

1. Presence of hemangiomas on skin or mucous membrane.
2. The frequent presence demonstrable by roentgen ray of phleboliths, homogeneous or layered in diffuse infiltrating cavernous hemangioma.
3. Significant association of intussusception with polypoid hemangiomas of small intestine.
4. Possibility of roentgen demonstration of indentations and constriction of the small intestinal lumen in cases of otherwise unexplained gastrointestinal hemorrhage.—*Russel R. Jauernig, M.D.*

Colvert, James R. Rectal polyps; diagnosis, five year follow-up and relation to carcinoma of the rectum. *Am. J. M. Sc.*, Jan., 1948, *215*, 24–32.

Rectal polyps rarely present symptoms suggestive of their presence and examination of the patient is incomplete without proctoscopic examination. Patients with rectal polyps should have a double contrast barium enema to rule out polyps higher in the colon.

One cannot be guided by size, shape or general appearance as to whether a polyp is malignant or benign although there is a much higher percentage of ulceration in malignant polyps. Only by prompt removal of a rectal polyp and pathological examination can one determine malignancy or benignity, and thus give patients a maximum chance of permanent cure without major surgery.

Prompt removal of the majority of rectal polyps in this group of cases resulted in a five year cure without any major surgery in 13 out

of 14 patients with malignant rectal polyps.—*Herbert Lobsenz, M.D.*

HARRINGTON, STUART W. Various types of diaphragmatic hernia treated surgically. *Surg., Gynec. & Obst.*, June, 1948, *86*, 735–755.

The reason for the different types of diaphragmatic hernias is the unusual embryologic formation of the diaphragm which makes for weak parts through which these hernias may occur.

Nontraumatic Hernia. A nontraumatic diaphragmatic hernia may be congenital or acquired. If it is congenital, the hernia is attributable to embryologic deficiency and usually does not have a hernial sac. The common sites of a congenital hernia, in the probable order of frequency of occurrence, are:

1. Through the pleuroperitoneal hiatus. These hernias occur in the posterolateral portion of the diaphragm and are due to failure of fusion of the pleuroperitoneal membrane and the septum transversum. The defect is usually triangular with the apex toward the median portion of the diaphragm. These hernias do not have hernial sacs and there is a direct communication between the abdominal and the thoracic cavity.

2. Through a gap left by partial absence of the diaphragm, a gap which is usually situated in the posterior portion of the muscle. These hernias may be considered an enlargement of the foregoing pleuroperitoneal type in that the essential difference is a much more extensive congenital defect in the formation of the diaphragm. There are more abdominal viscera involved than in the pleuroperitoneal hernia as the stomach and spleen, also the large and small intestine are often included.

3. Through the esophageal hiatus due to a deficiency of the circular muscle bundles of the hiatus.

4. Through the esophageal hiatus due to deficiency of the esophagus which is not elongated sufficiently to extend to the diaphragm thus causing varying amounts of stomach to remain above the diaphragm depending on the amount of shortening of the esophagus.

5. Through an anterior subcostosternal opening (foramen of Morgagni or Larrey's spaces). This is one of the two types of diaphragmatic hernia which have a hernial sac. The other type is that through the esophageal hiatus. These subcostosternal hernias are essentially direct hernias through a congenital defect in the structure of the diaphragm or faulty attachment of the diaphragm to the sternum and costal cartilages.

If the hernia is acquired after birth, the sites of occurrence are: (1) through the esophageal hiatus, a type in which there is a hernial sac, (2) through the region of fusion of the anlage of the diaphragm, and (3) at sites named under the congenital types of hernia.

Traumatic Hernia. Traumatic diaphragmatic hernia may be caused by direct or indirect injury or by inflammatory necrosis of the diaphragm. In cases of indirect injury of the diaphragm, the hernia may occur at any point, including points of embryologic fusion, but the most common sites are the dome and the posterior half of the left part of the diaphragm.

Rupture of the diaphragm may be the result of inflammatory necrosis, which, in turn, has been caused by subdiaphragmatic abscess. Again, rupture may follow necrosis caused by drainage tubes which have been introduced into empyema cavities.—*Mary Frances Vastine, M.D.*

MEYER, KARL A., ROSI, PETER A., and STEIN, I. F. Studies on vagotomy in the treatment of peptic ulcer. II. Clinical evaluation. *Surg. Gynec. & Obst.*, May, 1948, *86*, 524–529.

Thirty-five patients with peptic ulcer have had vagus section and have been followed clinically from six to fifteen months. Complete vagotomy causes immediate cessation of peptic ulcer distress with apparent healing of the ulcer. There are marked changes in gastric secretory and motor mechanisms following complete vagotomy. It is not certain to what extent the altered gastric function is permanent. Little is known of the effect of vagotomy on the other organs innervated by the vagi.

It is still too early to make a final evaluation of vagotomy in the treatment of peptic ulcer. Until more information is available concerning the incidence of recurrence of ulcer distress and the possible late sequelae, the use of vagotomy should be limited to clinical investigation, with one exception. Complete vagotomy is the method of choice in the treatment of marginal ulcer following gastric resection.—*Mary Frances Vastine, M.D.*

Stein, I. F., and Meyer, Karl A. Studies on vagotomy in the treatment of peptic ulcer. III. Physiological aspect. *Surg., Gynec. & Obst.*, Aug., 1948, *87*, 188–195.

Following complete vagotomy there is a marked reduction of the night secretion and the basal secretion. The secretory response of the stomach to caffeine and histamine is greatly reduced.

Insulin hypoglycemia produces an increase in gastric secretion and usually motility. This action is abolished by complete vagotomy. There are no spontaneous hunger contractions in the fundus of the stomach up to nine months following complete vagotomy.

The vagi are the sole mediator of the cephalic phase of gastric secretion. They are the most important factor concerned in the interdigestive period and a contributing factor in the gastric phase of secretion. Complete vagus section in some manner interrupts a mechanism necessary for chronicity of peptic ulceration.—*Mary Frances Vastine, M.D.*

Berg, Benjamin N. Gastric ulcers produced experimentally by vascular ligation. *Arch. Surg.*, Jan., 1947, *54*, 58–66.

In the past, attempts have been made at an experimental level to prove Virchow's hypothesis that human gastric ulcers were of vascular origin. For the most part, no significant results were obtained which was attributed to the fact that the experimental animal, dogs, had a highly efficient collateral circulation in the region of the stomach.

Rats had not been previously used for this experiment. They seemed ideally suited for it because the main gastric vessels do not communicate directly with one another as they do in dogs and in human beings.

Three groups of experiments were carried out, one in which the antral blood supply was ligated, a second in which unilateral ligation of the fundic vessels was accomplished and a third in which bilateral ligation of the fundic vessels was carried out.

Ten of the 18 rats in which the antral blood supply had been ligated developed punched-out penetrating ulcers. In contrast, when unilateral ligation of the fundic vessels was established, only 1 of the 12 animals so ligated revealed a ulcer. When bilateral ligation of the fundic vessels was established, 5 of the 8 animals used revealed similar ulcers. It was noteworthy that despite extensive gastric ulcerations, all the rats kept for periods of eight days or sixteen days survived ligation.

This suggests that a separate factor is concerned with involvement of the muscular coats of the stomach after the initial break of the mucosa has taken place.—*Philip J. Hodes, M.D.*

Ferrer, José M., Jr. The effect of tetra-ethyl ammonium chloride on gastric secretion and acidity in peptic ulcer. *Surg., Gynec. & Obst.*, July, 1948, *87*, 76–78.

The excessive secretion of acid gastric juice at night when the stomach is empty of food has been shown by Dragstedt to be a major contributing factor in the origin and particularly in the continuing activity of peptic ulcers. He has further shown that the amount of free stomach acid and the volume of the night gastric secretion are excessive in patients with peptic ulcer as compared with normal persons or patients with other diseases. To decrease this night secretion, Dragstedt devised an efficient method of sectioning the vagus nerves to the stomach. Following complete section of both vagus nerves, a marked decrease in the secretion of acid gastric juice has been uniformly observed. Unfortunately, however, the effects of vagus section have not been entirely beneficial. Many observers have reported postoperative gastric atony, dysphagia, bouts of diarrhea, etc.

Because of the unfortunate effects of vagus section the author conceived a method of temporary vagal block to effectively decrease the excessive night gastric secretion in the patient with peptic ulcer without interfering with vagal function during the day when acid gastric juice and peristaltic activity are needed in the processes of digestion.

Conclusions

1. Tetra-ethyl ammonium chloride (etamon) prevented excessive night gastric secretion and acidity in 12 out of 17 tests of patients with peptic ulcer.

2. Intramuscular etamon dosage of approximately 20 milligrams per kilogram of body weight is usually adequate to produce the desired effect if repeated at four hour intervals.—*Mary Frances Vastine, M.D.*

METZ, ARTHUR R. Duodenal regurgitation. *Arch. Surg.*, Sept., 1947, *55*, 239–245.

The author believes that duodenal regurgitation has not been given proper consideration as the cause for symptoms in recent years.

The symptoms vary with the degree of obstruction. When the obstruction is minimal recurring attacks of nausea with some disturbed appetite are common. With progression the nausea increases and is frequently attended by a sense of fullness in the right upper abdomen. Vomiting and ultimately considerable loss of weight ensue.

The diagnosis depends upon the demonstration by roentgen methods of a dilated duodenum associated with to and fro regurgitation of the barium which seems to stop abruptly in the region of the spine. The author believes that it is pressure by the mesenteric vessels on the duodenum where it passes over the spine in ptotic individuals that is responsible for the duodenal regurgitation.

The author has operated upon 14 patients with relief of symptoms. He believes the surgical treatment of choice following careful medical management is a duodenojejunostomy.—*Philip J. Hodes, M.D.*

HEIFETZ, CARL J., and SENTURIA, H. R. Acute pneumocholecystitis. *Surg., Gynec. & Obst.*, April, 1948, *86*, 424–433.

By acute pneumocholecystitis is meant an acute infection of the gallbladder characterized by the production of gas within the gallbladder lumen. The diagnosis is made roentgenographically, the gallbladder being visualized through the contrast medium of gas. That gas-forming organisms are frequent inhabitants of the biliary tract has been known for years. While a majority of normal and diseased gallbladders are sterile, others contain a wide variety of bacterial flora, headed in frequency by the *Escherichia coli communis* and the *Clostridium perfringens*. Besides these organisms other gas-formers, often difficult to classify, may exist in the bile tract. For the most part they seem to exist as harmless saprophytic inhabitants.

In evaluating the significance of the role of gas in acute pneumocholecystitis, certain considerations of etiological importance in ordinary cases of acute cholecystitis should be discussed. There is now rather universal agreement that a prime etiologic factor is obstruction at the out let of the gallbladder. Berk reported that blockage of the outlet of the gallbladder by calculi was found in over 92 per cent of the cases of acute cholecystitis collected from the literature.

It is likely that the infections of the gallbladder which produce gas are rarely associated with *Clostridium perfringens*, but instead with other gas-forming organisms. Another inference is that the development of acute cholecystitis in these cases occurs independent of the bacteria present, and the formation of gas is a rare complication which depends upon the presence of a gas-former within the gallbladder at the time, and, more important, upon conditions enhancing its gas-producing potentialities. That these poorly understood conditions are important can be adduced from the fact that many acute gallbladders contain *Clostridium perfringens* and other gas-forming organisms without producing gas.

Summary

1. Eight cases of acute pneumocholecystitis have been collected from the literature and reviewed. Two additional cases diagnosed preoperatively are added to the literature.

2. By pneumocholecystitis is meant acute infection of the gallbladder characterized by the production of gas within the gallbladder. Pericholecystic infiltration with gas may or may not be present.

3. Necrosis of the gallbladder with perforation is a frequent finding. However, the virulence of the infection is relatively less than in gas bacillus infections elsewhere in the body.

4. Bacteriologically, no constant distinctive organisms are demonstrable.

5. Surgical therapy alone is effective since the gallbladder wall is subject to greater tension when gas is present and there is a consequent greater risk of gangrene and perforation.—*Mary Frances Vastine, M.D.*

KITTLE, C. FREDERICK, JENKINS, HILGER P., and DRAGSTEDT, LESTER R. Patent omphalomesenteric duct and its relation to the diverticulum of Meckel. *Arch. Surg.*, Jan., 1947, *54*, 10–36.

This is a comprehensive and clearly written review of the history, embryology, anatomy and pathology of patent omphalomesenteric duct and the diverticulum of Meckel. In addition, the authors summarize the findings in 102 cases of patent omphalomesenteric duct reported in the literature and 26 additional cases in which prolapse of the intestine occurred through this structure.

According to the authors, Meckel's diverticulum and the patent omphalomesenteric duct are the consequence of the same defect in embryologic development, differing only in the extent to which the omphalomesenteric duct fails to obliterate. Whereas Meckel's diverticulum occurs in about 1 to 2 per cent, there were but 2 patients with patent omphalomesenteric ducts among the 30,000 births at the Chicago Lying-In Hospital of the University of Chicago during a ten year period.

Usually the defect is first noted at birth when a small red mass is seen at the umbilicus after the cord structures have sloughed away. The presence of fecal drainage is almost pathognomonic. The authors discourage the use of a probe because of the possibility of perforating the bowel and advise the introduction of radiopaque material through a small catheter in order to diagnose or exclude the congenital defect. The presence of a short communication which extends from the anterior abdominal wall down to the ileum is pathognomonic. The variant is three to four times as common in males as in females.

The patent ompthalomesenteric duct must be distinguished from granulation tissue in the stump of the umbilical stalk due to infection. A patent urachus with or without urinary discharge may be confused with it. In rare instances, a ligated loop of bowel which may have prolapsed into the umbilical cord may simulate the patent duct.

Operation for excision of the patent duct is advised as soon as the diagnosis is made in order to avoid the hazard of intestinal prolapse. When this complication occurs, the prognosis becomes increasingly unfavorable depending upon the duration of the prolapse.

This article contains a complete bibliography and of particular interest is the diagrammatic illustration of the different variations in the development of the omphalomesenteric duct which is included.—*Philip J. Hodes, M.D.*

Beneventi, F. A., and Twinem, F. P. Neuroblastoma. *J. Urol.*, Aug., 1948, *60*, 235–241.

Neuroblastoma is next in frequency to Wilms' tumor as the most common abdominal tumor in infancy and childhood.

The authors report the case of a twenty month old child who had developed an abdominal enlargement within two weeks following hospital discharge for an otitis media. This swelling increased rapidly and cervical nodes became palpable at the same time. On admission to the hospital the child had a fever of 101° F. and a hard palpable mass in the left side of the abdomen, extending from the costal border to the pelvis and well across the midline. Excretory urograms showed a normal right kidney and no demonstrable function on the left. A diagnosis of Wilms' tumor was made. At operation the left kidney could not be identified and the tumor mass was not removable. The patient died the day following operation. At postmortem examination the left kidney was incorporated in a huge tumor mass. The kidney pelvis was compressed but not invaded. The left adrenal gland could not be identified. The histopathological diagnosis was neuroblastoma.

Neuroblastoma is an extremely malignant, rapidly growing tumor, made up of undifferentiated neuroblasts. Virchow first separated these tumors from the sarcoma group and called them gliomas. Around 1900 the group was divided into Hutchinson and Pepper types, the former arising in the left adrenal and metastasizing to the skull and the latter arising in the right adrenal and metastasizing to the liver. These types are now felt to be unjustifiably separated. Wright, in 1910, first used the term neuroblastoma after Kuster had described the rosette formation of the cells in 1905.

Neuroblastoma can arise from the adrenal medulla or from sympathetic nervous tissue of other structures.

The clinical picture is that of a pale underweight infant or young child with a rapidly enlarging abdomen. In the differential diagnosis Wilms' tumor is the most difficult problem. Bone involvement in Wilms' tumor is rare and common in neuroblastoma. Neuroblastoma is more resistant to roentgen therapy.

Other lesions which may occasionally cause difficulty in the differential diagnosis include scurvy, adrenal cortical tumors, lymphosarcoma, ovarian tumors, leukemia and Ewing's sarcoma.

Farber, who has reported a series of 40 cases, believes that every solid tumor in infancy should be considered malignant until proved otherwise by pathological examination, and that the tumor should be removed within forty-eight hours with no delay for preoperative roentgen therapy. He recommended post operative roentgen therapy. Farber reported 25 per cent survival of from three to eight years. He also observed that these tumors may undergo spontaneous hemorrhage and necrosis

and disappear without any therapy other than biopsy. He also observed that these tumors may spontaneously mature into benign ganglioneuromas.—*Rolfe M. Harvey, M.D.*

MILLER, EDWIN. Malrotation of the colon. (Editorial) *Surg., Gynec. & Obst.*, Aug., 1948, *87*, 235–237.

The term "malrotation," strictly speaking, is that state of affairs that is present when either the normal counterclockwise rotation or the abnormal clockwise rotation of the midgut has been arrested before it is completed and one or more segments of bowel, usually the cecum, has become fixed by adhesions in an abnormal position.

From a clinical standpoint the end result is almost always an acute or chronic obstruction of the duodenum. Occasionally the onset of trouble is delayed for weeks, months or even years and occasionally the onset is insidious, but in great the majority of cases the picture is acute and comes on a few days after birth. The outstanding feature, of course, is the persistent vomiting of bile and it is usually associated with fullness in the epigastrium and flatness of the lower belly. If, however, the obstruction is incomplete and intermittent in character, the several loops of twisted midgut may contain much fluid and gas and a mass may be readily palpable.

Early surgery is the key to success and it consists essentially in untwisting a volvulus or completely severing abnormal adhesions associated with a malrotated colon. Through an ample incision the entire abdomen is explored. The distended duodenum is noticed at first glance and the absence of the colon in its normal place gives one an immediate clue as to the basic underlying pathology.—*Mary Frances Vastine, M.D.*

POTTS, WILLIS J. Congenital atresia of intestine and colon. (Editorial) *Surg., Gynec. & Obst.*, April, 1948, *86*, 504–506.

Atresia of the bowel is a rare congenital deformity which cannot be diagnosed until symptoms of obstruction appear. Vomiting is the first symptom. If the obstruction is high, persistent vomiting will begin shortly after birth; if the obstruction is near the ileocecal valve, the most common site, vomiting may not become alarming until the second or even the third day of life. Most atresias of the bowel are distal to the ampulla of Vater; the vomitus therefore is green. A newborn baby who vomits green material has intestinal obstruction until proved otherwise. It does not have pyloric stenosis because the vomitus of a baby with pyloric stenosis is never green.

Distention of the abdomen varies with the level of obstruction. One should not be led astray by finding a scaphoid abdomen in these patients. Progressive and finally marked distention of the abdomen, however, typifies atresias of ileum or colon.

The difference between a normal meconium stool and that of an infant with intestinal atresia is not great enough to be impressive.

The suspected diagnosis of atresia of the intestine or colon is easily confirmed by examination of roentgenograms made of the baby in the upright position. Widely distended loops of bowel showing fluid levels will be seen. The number of distended loops of bowel and their position in the abdomen will indicate the level of obstruction. These babies should not be given barium; its use is unnecessary for diagnosis, it tends to clog the intestine and if aspirated produces tracheobronchitis.

The treatment of congenital atresia of the intestine and colon is surgical.—*Mary Frances Vastine, M.D.*

SARNOFF, STANLEY J., ARROWOOD, JULIA G., and CHAPMAN, WILLIAM P. Differential spinal block; the investigation of intestinal dyskinesia, colonic atony, and visceral afferent fibers. *Surg., Gynec. & Obst.*, May, 1948, *86*, 571–581.

All patients studied were from the surgical services of the Massachusetts General Hospital. Five patients were given a differential spinal block in an attempt to alter temporarily bowel function. Two additional patients had the visceral afferent pathways (carrying the sensation of distention) tested while under the influence of a high differential block.

Conclusions

1. Visceromotor fibers to the intestinal tract are of about the same size and degree of myelination as other sympathetic efferent fibers insofar as this similarity is indicated by their relative susceptibility to procaine hydrochloride.

2. Block of sympathetic efferent fibers to the intestinal tract was followed by a definite increase in propulsive bowel activity and co-

ordination of transport in 3 of the 5 patients studied, and a probable alteration in bowel activity in the remainder.

3. Visceral afferent fibers subserving the sensation of distention are relatively large, myelinated axones insofar as this is indicated by their relative refractoriness to procaine hydrochloride. They are not blocked by that concentration capable of interrupting sympathetic efferents (vasomotor, sudomotor and visceromotor) and fibers carrying the appreciation of pinprick.

4. Impulses traveling over autonomic nerves can contribute significantly to the production of a syndrome consisting of distention, obstipation, tympanites, fecal vomiting, and cramp-like abdominal pain which can be easily confused with acute, mechanical, intestinal obstruction. This type of neurogenic obstruction may be sufficiently obscure to precipitate numerous abdominal interventions and the patient finally falls into that category labelled "the multiple laparotomy syndrome."

5. The conventional type of full spinal block and a differential spinal block are of value in relieving this type of bowel obstruction, and in helping to establish the diagnosis. The differential spinal block is more specific as an investigative tool inasmuch as the fibers carrying distention pain are not interrupted. The alteration of bowel activity is therefore presumably due to a block of visceromotor fibers. It has the added advantage of allowing the patient to use her abdominal musculature in expelling colon contents at the peak of intestinal activity.

6. Impulses arising in the autonomic nervous system may be important in colonic atony as seen in the adult, since block of the visceral efferents can greatly alter colon activity in such a patient.

7. It is of great importance to withhold medication when attempting to augment intestinal activity and transport by means of spinal anesthesia.—*Mary Frances Vastine, M.D.*

Leithauser, D. J. Atypical adynamic ileus apparently caused by nutritional (thiamine chloride) deficiency. *Surg., Gynec. & Obst.*, May, 1948, *86*, 543–550.

The cases of 6 patients with adynamic ileus with severe abdominal distention are reported to call attention to the fact that symptoms suggesting the presence of intestinal obstruction may be caused by thiamine chloride deficiency. In these cases, the distention was not controlled by mechanical decompression or administration of prostigmine but responded dramatically to administration of thiamine chloride and vitamin B complex.

In the first case in which the condition was recognized as resulting from vitamin deficiency, the patient had a sore mouth which directed attention to this possibility. Specific questions brought to light a history of chronic alcoholism. In this instance, a preoperative diagnosis of "annular carcinoma of the sigmoid" had been made on the basis of obstructive symptoms and the roentgenographic findings but no such lesion was found at operation. However, the abdominal distention increased after operation and was not brought under control until vitamin therapy was instituted. The second patient, also an alcoholic, was subjected to celiotomy for "acute appendicitis," but at operation there was so much intestinal distention that the appendix was not readily accessible and was not removed. When uncontrollable distention continued after operation the experience in the first case was recalled and vitamin therapy was instituted, with equally striking results.

The author suggests that nutritional deficiency should be suspected and a therapeutic trial of vitamins made in cases of abdominal distention in which the evidence does not justify a positive diagnosis of mechanical obstruction of the intestines. He suggests also that thiamine chloride should be administered at the time of operation to prevent postoperative distention, especially in patients whose nutritional status is at all questionable or in whom there is any suspicion of liver damage.

It is the writer's routine practice to administer parenterally vitamin B complex with high thiamine content to all surgical patients the day before operation, and daily for three days after operation. Since this has been done, postoperative distention has been almost entirely eliminated.—*Mary Frances Vastine, M.D.*

GENITOURINARY SYSTEM

Antopol, W., and Goldman, Lester. Subepithelial hemorrhage of renal pelvis simulating neoplasm. *Urol. & Cutan. Rev.*, April, 1948, *52*, 189–195.

Seven cases with hematuria are presented in which pyelograms showed filling defects in the kidney pelvis suggesting renal neoplasm. The right kidney was involved in 6 of these cases.

In the extirpated specimen the pelvic defects

were found to be due to subepithelial hemorrhage of the renal pelvis. Superficial cortical infarctions were present in 5 of the cases. The subepithelial hemorrhage is obviously due to vascular injury. There was definite history of trauma in only 2 of the cases. The authors feel that because the pelvis and hilar blood vessels are poorly supported in the sinus of the kidney it might require only minimal trauma, even the inertia of the kidney, due to sudden changes of position or motion, to produce this lesion. This view may be supported by the fact that 6 of these 7 cases were found in the more mobile right kidney. Four of the cases also exhibited congenital malformations consisting of (1) extrarenal pelvis, (2) faulty ureteral insertion, (3) bifid pelvis and double ureter and (4) aberrant vessels with extensive fetal lobulation. The authors feel that these congenital abnormalities might predispose to or exaggerate insults to the organ.

The cases are difficult to evaluate by single roentgen examination. Since pelvic hemorrhage may be absorbed, a later examination may show regression to normal. The authors believe that retrograde pyelograms should be taken after partial filling due to the rigidity and inelasticity of these pelves.—*William G. Johnson, M.D.*

HALE, NATHAN G. Primary papillary carcinoma of the ureter; report of 2 cases. *Urol. & Cutan. Rev.*, Jan., 1948, *52*, 3–7.

The author presents 2 cases of primary ureteral papillary carcinoma along with an excellent historical review and discussion of the lesion. In 1936 Rusche and Bacon concluded there were 93 cases of proved primary carcinoma of the ureter. Review of the literature to date reveals 198 cases. The majority of cases are between the ages of sixty and eighty.

The diagnosis of this lesion is usually made at operation. Only 7 cases have been diagnosed preoperatively, the usual diagnosis being functionless kidney or non-opaque calculus. There was no dye shadow found on the affected side in one-half of the 18 cases reported by Cook and Counseller in 1941. In 35 per cent of their cases the ureteral tumor was visible at the bladder orifice. A suggested aid to diagnosis is the passage of a small catheter and taking serial ureterograms at various levels. The increase of reports of this lesion in the past decade suggests improved diagnostic methods better applied.

All treatment has been disappointing. Only 1 patient survived over five years in the 45 cases reviewed in the past nine years. Metastases are widespread due to the abundant lymphatic supply of the ureter. Metastasis has been reported in lungs, liver, bones, bladder, lymph nodes and female genital organs. In 25 per cent of the cases implants have been found in the bladder either before or after diagnosis.

Nephro-ureterectomy with removal of the bladder cuff in one stage is the operation of choice. Neither of the 2 cases reported by the author had the bladder cuff removed. Roentgen therapy as a postoperative adjunct is questioned although the author states his knowledge of its real worth is meager.—*William G. Johnson, M.D.*

MELICK, W. F., and VITT, A. E. The present status of aortography. *J. Urol.*, Aug., 1948, *60*, 321–333.

The authors summarize the literature dealing with early attempts to visualize the circulatory tree. The original reports in experimental animals were unfavorable because of high mortality rates. Fariñas made aortograms by passing a catheter up the femoral artery and injecting 70 per cent diodrast. In 1942 the translumbar method of injection was introduced. The authors have not found one fatality in over three thousand reported injections using this method.

The technique of the translumber route consists of insertion of the needle just below the twelfth rib, four fingerbreadths to the left of the spine. The needle is directed medially and superiorly until the vertebral body is encountered and then withdrawn slightly and directed laterally just past the body into the aorta. The authors state that there are no other important structures which might be hit accidentally. Occasionally, in arteriosclerotic individuals, bleeding may result from strking an atheromatous plaque. A pressure system, rather than hand injection, is used. An ideal medium has not been found. Seventy per cent diodrast does not outline smaller arteries well. The medium employed by the authors is 80 pei cent sodium iodide. Iodism and allergic reactions have occurred.

Aortography should not be employed in the presence of severe liver damage, nephritis, uremia, or in the presence of iodine sensitivity. The authors test for sensitivity by injecting a few drops of the medium intravenously and they routinely give 1,000 cc. of normal saline containing 500 mg. of vitamin C intrave-

nously following aortography. The injection is performed under general anesthesia. A high speed Bucky and a 500 ma. capacity tube are required for short exposures.

The particular value of aortography is in the following groups of cases:

1. Ureteral blockage associated with nonfunctioning kidneys.
2. Extraperitoneal tumors.
3. Renal hematuria with a normal pyelogram.
4. Renal hematuria with a deformed pyelogram.
5. Renal tumors to determine operability.
6. Hydronephrosis due to aberrant vessels.
7. Renal anomalies to determine the length of the renal pedicle.
8. Hypertension to show renal blood flow and relative renal mass.
9. Renal cysts.
10. Placental visualization in pregnancy.—*Rolfe M. Harvey, M.D.*

Edelstein, J. M., and Marcus, S. M. Primary benign neoplasm of the ureter. *J. Urol.*, Sept., 1948, *60*, 409–417.

The authors summarize the cases of benign neoplasms of the ureter which have been reported. They found a total of 27 verified cases and rejected an additional 16 cases in which the diagnosis was not verified.

They report the case of a sixty year old white male who had complained of hematuria for three years. A ureteropyelogram showed a large filling defect in the left mid-ureter, 2 cm. in diameter. The ureter was removed together with the left kidney. A papilliferous tumor mass was found in the ureter and a histopathological diagnosis of transitional type papilloma was made.

The commonest symptoms of ureteral tumors are hematuria, which occurs in 75 per cent of cases, pain and enlargement of the kidney on the affected side. A ureterogram is essential for the diagnosis. Malignancy, tuberculosis, calculi and strictures must be ruled out. Ureteronephrectomy is the accepted treatment.

The authors classify benign tumors of the ureter as (A) epithelial: papilloma; and (B) non-epithelial: myoma, lipoma, fibroma, hemangioma, etc.—*Rolfe M. Harvey, M.D.*

Campbell, Meredith F. Congenital hydronephrosis and hydroureter. (Editorial) *Surg., Gynec. & Obst.*, Aug., 1948, *87*, 237–239.

About 12 per cent of all individuals are born with some variety of urogenital tract malformation and of these approximately one in six has congenital obstruction in the upper urinary tract. Renal excretion begins between the fifth and sixth month of fetal life and for this reason, when obstruction exists, advanced hydronephrosis and other urinary backpressure damage often exists at birth.

Stricture is by far the commonest congenital urinary obstruction. This includes congenital contracture of the vesical outlet. Aberrant renal vessels sometimes compress the ureter. Occasionally the ureter is compressed by congenital bands or ureteral diverticulum.

Congenital ureteral stricture occurs most often at the pelvic junction. This, as well as congenital stricture in other body systems such as the biliary and intestinal tracts, is simply an anomalous narrowing of the lumen. These strictures usually involve only a short section of the ureter. In some cases only renal exploration will demonstrate whether the obstruction is due to stricture, aberrant vessel blockage at the pelvic outlet, ureteral compression by fibrous bands, enlarged lymph nodes or purulent collections.

Stricture below the ureteropelvic level occurs predominantly at the ureterovesical junction where it is bilateral in about a third of the cases. As a rule, the dilation is greatest just above the stricture and this often acts as a buffer to spare the kidney the full harmful effects of the urinary backpressure.

About 25 per cent of all kidneys have an anomalous blood supply with aberrant arteries, veins or both passing from the upper pole, laterally from the cortex, or downward or upward and medially from the lower pole. The last group often cause obstruction of the upper ureter.—*Mary Frances Vastine, M.D.*

McGavran, H. G. Giant prostate without symptoms: neurofibroma. *J. Urol.*, Aug., 1948, *60*, 254–259.

The author reports the case of a giant prostate because of its extreme size, the fact that the tumor was not an adenoma, the fact that the tumor did not produce symptoms of prostatism, and finally because erosion of the pubis resulted from the huge size of the tumor.

The patient was a forty-four year old male who had had a five year history of right lower back pain radiating down the right leg. Roentgenograms of the back and hip were repeatedly negative. There were no urinary symptoms.

By rectal examination a smooth tumor mass was felt, too large to permit passage of the finger beyond it. The mass could be palpated abdominally three fingers above the symphysis.

A cystourethrogram showed marked displacement of the bladder upward and to the left. There was a marked indentation on the bladder wall from tumor pressure. The body and superior ramus of the right pubic bone was almost completely eroded. At operation a huge prostatic tumor was removed. A small bone sequestrum came out with the tumor. Postoperative roentgenograms showed gradual ossification of the os pubis following postoperative roentgen therapy, which was given for nine days (dosage not stated). The pathological report was neurofibroma. The tumor weighed 839.5 grams. This is the second largest benign tumor of the prostate which has been reported.—*Rolfe M. Harvey, M.D.*

BEATTY, R. P. Life expectancy in carcinoma of prostate; a five year survey of eighty-eight cases. *J. Urol.*, Aug., 1948, *60*, 264–268.

This is a supplementary report on 20 additional cases of prostatic cancer, the author having previously reported 68 cases. The diagnosis was made, when biopsy was not secured, on the presence of weight loss, anemia, elevation of the serum acid phosphatase, presence of a fixed hard prostate by rectal examination and roentgen evidence of bone metastases.

Fourteen cases of the recent series had roentgenograms of the spine and pelvis, but only 4 showed evidence of metastases, in spite of the fact that 12 had elevation of the serum acid phosphatase. Of the entire series of 88 cases, 35 are still living and 26 are known to be dead. The average survival rate of the cases which have been followed is 2.73 years for the known dead cases, and two years for those who are still alive.—*Rolfe M. Harvey, M.D.*

SKELETAL SYSTEM

HAUSER, EMIL D. W., and CONSTANT, GEORGE A. Skeletal hemangio-endothelioma; a case report. *J. Bone & Joint Surg.*, April, 1948, *30A*, 517-521.

A case of skeletal hemangio-endothelioma in a white woman, forty years old, is reported which demonstrates some of the complications encountered in diagnosis and treatment of the condition. The patient is still living, nine years after the diagnosis was confirmed. A single lesion was shown in each hip and the question arose as to whether there are two primary lesions, or whether one was a metastasis. The history and course of the case led to the opinion that there were two primary lesions.

Roentgenograms revealed a cystic lesion in the neck of each femur with an ununited pathological fracture, sustained one year previous to admission to the hospital, in the right. Serial studies later showed increased destruction of both femurs with invasion of the surrounding soft parts.

The authors believe that any skeletal lesion, which appears in the roentgenogram as cystic, trabeculated, with invasion of the surrounding soft parts, merits the consideration of skeletal hemangio-endothelioma in the differential diagnosis. Surgical intervention is the only procedure that at present offers any benefit. Roentgen therapy did not resolve the lesion.

Nine years after operation the tumor had increased in size and had invaded the entire pelvis. In spite of the enormous size of the tumor and the pathological fracture of the right femur, the patient is able occasionally to be up in a wheel chair. No metastases were found when the patient was last examined.—*R. S. Bromer, M.D.*

FAIRBANK, H. A. THOMAS. Osteopetrosis; osteopetrosis generalisata, marble bones; Albers-Schönberg's disease, osteosclerosis fragilitas generalisata. *J. Bone & Joint Surg.*, May, 1948, *30B*, 339–356.

This paper includes a short description of the familial and hereditary tendencies, the sex incidence, age of occurrence and etiology of osteopetrosis. Included also, at somewhat greater length, are discussions of the clinical features, roentgenographic features and pathological changes of the disease with a paragraph on the diagnosis from a differential standpoint. Seven cases are described with numerous reproductions of the roentgen findings.

A distinct familial tendency is found and the disease is occasionally inherited. It affects both sexes and is found at all ages from fetal life to seventy-five years. It undoubtedly begins before birth in some cases and possibly in most. The cause is unknown. The chief features of the syndrome are abnormal density of the bones with or without fragility, a strong tendency to anemia which may be severe and fatal, and optic atrophy. In some cases there is a tendency

to fracture, but, on the whole, fragility of the bones has been much exaggerated. When they occur, fractures are sharp, abrupt and transverse. The anemia results from reduction of the blood-forming marrow in the sclerosed bones and eventually becomes of the aplastic type. Cases in which it was leukemic and even apparently pernicious in type have been described.

As seen in roentgenograms, the extent to which bones are affected varies considerably. The whole of a bone including the epiphyses may be uniformly dense and completely structureless. Fine striations, both transverse and longitudinal, may be seen in the metaphyses and epiphyses. Occasionally less dense areas may be seen in the sclerosed bone. The parts unaffected by petrosis may show osteoporosis but this is sometimes more apparent than real. As a rule, the metaphyses are more affected than the shafts of the long bones; they are commonly enlarged or clubbed, the enlargement ending abruptly at its junction with the diaphysis. Occasionally the reverse holds good, the diaphysis being more affected, with the metaphyses less dense and either normal or clubbed. A streaky or patchy arrangement of the denser bone is very rarely seen in cases of generalized osteopetrosis. Apart from the clubbing, the shape of the bones in both varieties is unaffected. In some cases a narrow clear transverse band marks the junction of the diaphysis and the enlarged metaphysis. If, in a child, the tendency to form petrosed bone ceases suddenly after a time, the epiphyses will show a dense center surrounded by a halo of normal density. The ilia often show alternating dense and clear curved bands parallel to the crests. The carpal and tarsal bones, although sometimes universally dense or mottled, frequently show a dense center surrounded by a halo of clearer bone; or the reverse may be seen when the pathological change began later than usual. As a rule the phalanges are decidedly less affected than the rest of the skeleton and they show a dense transverse band of varying width in the metaphysis, close to, or a short distance from, the epiphyseal lines. The skull shows density which is particularly marked at the base. The pituitary fossa is usually rather small, and the posterior clinoid processes are thick and clubbed, almost closing in the fossa. The air sinuses are invisible and the frontal and nasal bones may be thickened as well as dense. The maxillae may be affected but the mandible almost invariably escapes. Calcification of the dural folds may be seen. The vertebral bodies, if not uniformly dense, usually present two horizontal bands of dense bone above and below, with a less dense band between. The ribs are affected, sometimes irregularly, but the rib cartilages escape.

The diagnosis is usually easy when the roentgen examination has once been decided upon. In mild cases, chronic poisoning with lead or phosphorus must be excluded, while in certain localities, fluorosis is worthy of consideration. Juxta-epiphyseal bands of increased density in the metaphyses have been reported in cretins which disappeared under treatment. Occasionally, limited distribution of the dense bone may give rise to difficulty in classification; such cases are probably best placed according to Fairbank, in the melorheostosis group.

The roentgenograms of the reported cases are well worth study.—*R. S. Bromer, M.D.*

Fejer, E. Über einen interessanten Fall von Melorheostosis. (An interesting case of melorheostosis.) *Acta radiol.*, 1948, *29*, 112–116.

A case of melorheostosis affecting the left arm is reported. This is the twenty-sixth case reported in the medical literature. The author believes that a previous skull injury with trauma to a nerve trunk was responsible for the melorheostosis. He believes that a parathyroid dysfunction was caused by the skull trauma and that the melorheostosis developed secondarily to this dysfunction. Emphasis is laid on the importance of trauma to the skull in melorheostosis.—*Mary Frances Vastine, M.D.*

Alderson, B. Roxby. Further observations on fracture of the first rib. *Brit. J. Radiol.*, Sept., 1947, *20*, 345–359.

Many variations in the first rib have been shown in mass chest examinations and these have been described as fracture, anomaly, synchrondrosis, pseudarthrosis, anomalous development simulating fracture, and idiopathic fracture. Actually fracture of the first rib is much more common than is generally accepted. It occurs frequently from muscular violence, and may result in complete union, or nonunion and formation of a false joint. Often there is sufficient pain for a patient to consult a physician, but more frequently there is not. A series of 77,607 British males was examined and 73

fractures of the first rib were found. Four times as many were seen in individuals between the ages of seventeen and twenty as in those over twenty-five years. If the abnormalities described were congenital or developmental the incidence should be the same in the two groups. Approximately 70 per cent of the cases were available for interrogation. Of these one-quarter admitted symptoms referable to the area. Of the rest, with no history, one-third had previous or subsequent roentgenograms which, when submitted to comparison, revealed either a previously normal rib or evidence of subsequent healing.

These fractures are rarely the result of pressure transmitted from the clavicle. The great majority are best classified as stress fractures and are due to muscle strain.—*E. F. Lang, M.D.*

BRAILSFORD, JAMES F. Some experiences with bone tumours. *Brit. J. Radiol.*, April, 1947, *20*, 129–144.

In the diagnosis of bone tumors a combination of clinical and roentgenographic evidence alone permits of the most accurate diagnosis and this evidence can be obtained without causing the patient pain and without disturbing the lesion, as by biopsy. In some cases repeated examination and observation are necessary before a definite decision can be made, but this is not a serious disadvantage and may even be an advantage. In the author's experience when the clinical or roentgenographic evidence is indefinite the histopathological evidence is at least equally indefinite and may only add confusion. The only time a biopsy is excusable is when it provides material to support clinical and roentgenological evidence of simplicity. On the other hand, amputation on the basis of a biopsy which shows malignancy without conclusive other evidence is to take an unjustifiable risk. Experience with cases which underwent amputation for malignancy and with those in whom amputation for a lesion which was subsequently found to be benign indicates that there is nothing to be gained by undue haste and precipitate amputation, but much can be gained by observation of the clinical features and serial roentgenograms. The author has not seen a cure result from amputation when there is typical roentgen evidence of an osteogenic sarcoma.

There is also the question of who is to interpret the films. The growing tendency for the clinician to use his own interpretation is to be decried. The radiologist, by learning and practice, has fitted himself for this. The clinician can make the roentgen examination most valuable by supplying important information which the radiologist must consider in his study of the films if he is to interpret correctly the roentgen changes in each case. In an attempt to develop young radiologists of the type who can best aid the clinician in his problems it is essential that these young men be given a thorough knowledge of all the roentgen features met with in all the specialties. The author believes this training should be given at the expense of the unnecessary training in radiation physics.

The principles stated above in the management of bone tumors are illustrated by a presentation of cases with excellent reproductions of their roentgenograms, and a critical discussion of each csae.

A fourteen year old girl who had suffered a blow to her arm seven weeks previously and whose roentgenogram had been interpreted elsewhere as showing Ewing's sarcoma was seen and conservative therapy was advised. The lesion disappeared on antiluetic therapy. The basis for conservative treatment was the impression that the appearance of the bone seven weeks after trauma was not consistent with the effects of trauma for that period. The time factor is important in determining whether or not a given bone lesion could be due to antecedent trauma.

A six year old girl was seen with a painful swelling over the upper part of the right arm with disintegration of the structure of the humerus, periosteal reaction, and multiple rounded secondary pulmonary lesions. Since surgery was hopeless, sulfathiazole was advised, but without apparent benefit as shown on serial film studies. Three months later, however, improvement began, and three months after this an examination showed resolution of the osseous changes and complete disappearance of the pulmonary lesions.

A twenty-five year old male was seen complaining of a lump in the midthigh which was not tender but which was associated with some destruction of the femur and new bone formation, suggesting malignancy. Roentgen therapy was administered. One year later a somewhat similar lesion was observed in the upper portion of the femur and this again was treated by irradiation. Six months later a destructive lesion developed in the left transverse process of the

fifth lumbar vertebra. The limb was amputated; the section showed secondary carcinoma, probably of a bronchial origin. Six months later another lumbar transverse process was involved. Six months later there were multiple metastases in the ribs, vertebrae, and pelvis. Chest films had been made since the patient had first been seen but it was not until this time, two years and nine months after the first metastasis, that lesions were found in the pleura from the primary in the lung.

Other instructive cases indicating the value of careful consideration and correlation of the clinical findings and serial roentgen examinations, which cases illustrate the wisdom of the avoidance of biopsy or other disturbance of the bone lesion, are included.—*E. F. Lang, M.D.*

Shackman, Ralph, and Harrison, C. V. Occult bone metastases. *Brit. J. Surg.*, April, 1948, *35*, 385–389.

In over half of the patients dead of malignant disease with bone metastases which were examined at autopsy, gross evidence of metastatic tumor tissue in bone was present, although roentgenographic examination before death and direct contact radiographs made of the bone before section revealed normal bony architecture. Four cases are presented with microphotographs, contact radiographs, and colored photographs of the sectioned bone. Blood borne metastatic growths are situated initially in the bone marrow, most frequently in bones containing red marrow. True bone change which is secondary to the presence of cancer cells is effected by the osteoblasts and osteoclasts and occurs only after the marrow spaces have been infiltrated and probably filled. Roentgenograms taken during life at greater distances and through superimposed soft tissues would be less likely to reveal metastatic deposits. So-called normal roentgenograms cannot exclude the presence of even extensive bone metastases.—*Charles W. Werley, M.D.*

Hitchcock, Harold H., and Bechtol, Charles O. Painful shoulder; observations on the role of the tendon of the long head of the biceps brachii in its causation. *J. Bone & Joint Surg.*, April, 1948, *30A*, 263–273.

The authors state that lesions affecting the tendon of the long head of the biceps brachii are among the more frequent causes of pain and disability in the region of the shoulder joint. In the majority of cases, common predetermining factors are responsible for the several pathological conditions encountered. Of these factors, the most significant are the presence of the "supratubercular ridge" of Meyer, described in 1928 and a preternaturally shallow bicipital or intertubercular sulcus which, with excessive function or as the outcome of trauma, results in a variety of lesions. These include acute or chronic peritendinitis, varying degrees of attrition and damage to the tendon, and its partial or complete dislocation.

The supratubercular ridge of Meyer is a ridge of bone, projecting immediately proximal to the medial wall of the bicipital groove and continuous with it. The biceps tendon is limited by this structure from slipping inward and is forced upward against the transverse humeral ligament, thus favoring dislocation. In their study, the authors included all ridges which they judged were high enough to force the biceps tendon against the roof of the groove and thus cause trauma to the tendon. They conclude that the normal anatomical mechanics of the biceps tendon are faulty. A supratubercular ridge or flat bicipital groove increases the mechanical difficulties.

An operation to fix the tendon in the bicipital groove and to remove that portion of the tendon above the groove relieves the symptoms caused by it and does not materially weaken the shoulder.—*R. S. Bromer, M. D.*

Davies, H. The unstable semilunar bone. *Lancet*, May 29, 1948, *1*, 831.

The carpal semilunar bone is not locked in its ball and socket position between the os magnum and the radius. It occupies a medial unstable position centered over the radioulnar joint. Its dorsal surface is reduced in size, and its articular facet for the os magnum lies obliquely. All these factors contribute to its instability and explain how pressure through the os magnum can so readily produce dislocation. It is remarkable that medial dislocation does not occur more often.—*J. S. Summers, M.D.*

Immermann, E. William. Dislocation of the pisiform. *J. Bone & Joint Surg.*, April, 1948, *30A*, 489–492.

Dislocation of the pisiform is a rare entity. It is still more rare to have chronic recurrent dislocation of the pisiform. The author believes

his case to be the first complete description of such an entity.

Dislocation of the pisiform may result either from a direct injury or from muscular violence. In the cases reported in the literature, the ratio was two to one in favor of muscular force as an etiological agent. This force in all instances was manifested as the patient was in the process of lifting a heavy object. Clinically, following a dislocation, the pisiform is painfully displaced from its normal site, leaving a depression. Flexion and adduction may be painful, and there may be exaggerated mobility of the bone. The diagnosis can be confirmed by roentgenograms, with the ulnar side of the wrist placed against the film in about 15 degrees of supinated rotation. It must be borne in mind, however, that in an acute or recurrent dislocation the bone may return to its normal position, producing a negative roentgenogram. In the chronic case, such as that of the author, where the patient complains of pain in the volar aspect, of the wrist with a sensation of "giving away" upon lifting, duplication of the etiology may confirm the supposed diagnosis.

In acute cases which do not respond to splinting, and in chronic cases, surgical excision is indicated. Removal of the bone in no way interferes with the normal function of the wrist. In an acute dislocation, the bone should be manipulated into place, and splinting should be applied using an anterior molded plaster splint.—*R. S. Bromer, M.D.*

ANDREASEN, A. T. Congenital absence of the humeral head; report of two cases. *J. Bone & Joint Surg.*, May, 1948, *30B*, 333–337.

The author states that the purpose of this article is to present clinical data, review the literature, and speculate as to the origin of a rare condition. The first case, he reports, had been passed over with the remark that "the condition is probably congenital." Attention was aroused when a second case was seen a few months later. Only 6 cases with similar roentgen appearances could be collected from the literature. In most of the cases other skeletal deformities were present, whereas in his cases only the shoulder was affected. The essential feature of the 2 cases was complete or incomplete absence of the humeral head with a rudimentary glenoid. The deformity may be unilateral or bilateral. It may be isolated or it may be one of a number of deformities in the same patient. It is associated with relatively slight disability. The ball and cup arrangement of the shoulder joint is reversed or it is replaced by a saddle-shaped articulation. There seems to be correspondence between the degree of capital deficiency and the state of development of the glenoid. It appears that lack of the capital epiphysis, or its cartilaginous and precartilaginous stages, causes a corresponding lack of the upper epiphysis of the glenoid-complex while the main body of the glenoid continues to develop.

Consideration of his 2 cases, together with experimental data from the studies of Fell and Canti, suggests that the time in development at which the fault occurred was the presumptive joint stage, just when the articular rudiments had separated.—*R. S. Bromer, M. D.*

MCDONNELL, D. P., and WILSON, JOHN C. Fractures of the lower end of the humerus in children. *J. Bone & Joint Surg.*, April, 1948, *30A*, 347–358.

This paper is based on a study of 176 fractures of the lower end of the humerus in children. Eighty-eight of the number were followed long enough to draw some general conclusions with regard to treatment and complications. Of the latter group, 55 were in boys and 33 in girls. The ages of the patients ranged from one to twelve years, the average age being seven. There were 53 supracondylar fractures, 33 lateral condylar fractures, 1 medial epicondylar fracture, and 1 epiphyseal separation of the capitellum.

Contrary to prevailing opinion, the authors believe supracondylar fractures can produce serious growth disturbance if the fracture lines extend into the epiphyseal centers. Cubitus varus and cubitus valgus are not considered serious disabilities, if flexion and extension are complete. However, if the deformity is progressive and is caused by disturbances in the growth centers, disabilities and limitation of motion may occur years after the initial injury. Supracondylar fractures in which the fracture line, or part of it, extends into the epiphyses may produce growth disturbances similar to those which result from fractures of the lateral and medial condyles. It the fragment is intra-articular and not attached to the overlying bone and soft tissue, it will undergo vascular necrosis. Fractures of this type should have an accurate anatomical reduction, and if the fragments are displaced and rotated, an open re-

duction is probably the best method of obtaining accurate alignment.

In lateral condylar fractures, avascular necrosis of the capitellum will occur if the fracture line separates the epiphysis from the overlying bone and soft tissues. Early open reduction with minimal trauma to soft tissues will give the best results. Fractures of half of the capitellum occurred in 2 patients with lateral condylar fractures. One had poor apposition by open reduction, and avascular necrosis occurred in one year. In the other, the separation was not complete, the position was good, and healing was uneventful.

Avascular necrosis of the trochlea may occur, later, despite good reduction of a supracondylar fracture. It can cause stiffness at the joint, due to thinning of the cartilage and distortion of the articular surface of the humerus.

Delayed ulnar palsy may cause progressive growth disturbances, and was present in 2 cases of severe cubitus valgus deformity.

Fracture of the medial epicondyle will not cause a serious disability unless the fragment enters the joint cavity. Non-union is difficult to avoid in closed reduction.—*R. S. Bromer, M.D.*

Andreasen, A. T. Avulsion fracture of lesser tuberosity of humerus; report of a case. *Lancet*, May 15, 1948, *1*, 750.

A woman fifty-six years of age was dismounting from a side saddle when her foot slipped. Since the right hand retained a grip on the saddle post, there was trauma to the shoulder with the arm fully abducted above the shoulder, the hand being fixed, and the body moving. This resulted in an avulsion fracture of the lesser tuberosity as proved by roengtenograms.

Operation was refused by the patient. The bone fragment first underwent aseptic necrosis, then was adsorbed in fourteen months. A study of the literature failed to reveal any similar case and this is thought to be a rare injury. Reproductions of the roentgenograms clearly show the avulsed fragment lying inferoposteriorly to the head of the humerus.—*J. S. Summers, M. D.*

Shellito, John G., and Dockerty, Malcolm B. Cartilaginous tumors of the hand. *Surg., Gynec. & Obst.*, April, 1948, *86*, 465–472.

Cartilaginous tumors of the hand (1) interfere with function, (2) are a source of potential malignancy, and (3) are unsightly for cosmetic reasons. It was found, on reviewing the literature, that all too often cartilaginous tumors are lumped together under the heading "osteochondroma" and the suffix "sarcoma," added to denote malignancy. It was discovered that it is correct, on the basis of pathology, to divide these tumors into two types: the enchondroma, or chondroma, and the ecchondroma.

Roentgenographic Observations

Enchondroma. The roentgenographic picture of these tumors caused the roentgenologist to suspect the presence of chondroma in 50 per cent of the cases. The typical picture was that of the so-called bone cyst which was seen as a small, round area of decreased density in the center of the bone. The cortex usually was expanded and thinner than it normally is. The outline was round and regular and appeared in the center of the shaft.

Ecchondroma. In contrast, the roentgenologist was able to make the diagnosis in almost all of the cases of ecchondroma. The lesion in this case appears at the periphery and one end of the bone. The bony elements of the base of the ecchondroma show plainly as an elevation of bony structure.

Summary and Conclusions

1. Cartilaginous tumors of the hand, on the basis of pathology, may be divided into two types: enchondroma and ecchondroma. The synonym for enchondroma is chondroma. Ecchondroma is called "perichondroma," "osteochondroma," and "exostosis." (The word "osteochondroma" is restricted to the ecchondroma.)

2. The fact that the entire group of cartilaginous tumors is commonly called osteochondroma has led, both in the past and in the present, to a great deal of confusion. It is better to use the terms enchondroma and ecchondroma.

3. Distinction between the two cannot be made with slide and microscope alone.

4. An enchondroma is usually a small cartilaginous tumor located centrally in the bone shaft, growing from many centers and expanding in all directions. Rate of incidence of pathologic fracture in our series was 26.6 per cent. The enchondroma occurs much more often in the hand than does the ecchondroma (3:1). These tumors, in comparison to normal hyaline

cartilage, show increased vascularity, calcium deposition, and myxomatous degeneration.

5. Two tumors of the tendon sheaths were found, both of which were enchondromas. In one of these cases multiple enchondromas of the sheath had developed and this is good evidence that an enchondroma can occur in the tendon sheath away from the site of tendon insertion.

6. The ecchondromas occur peripherally in bone near the end of the shaft and have a bony base and cartilaginous cap.

7. Either type of tumor may be malignant, in which case it is usually a sarcoma. In this series 2 per cent were malignant. Both types are prone to recur, although recurrence does not mean malignancy unless a mitotic figure can be found.

8. The treatment in both types is conservative operation. —*Mary Frances Vastine, M.D.*

UMANSKY, A. L., SCHLESINGER, P. T., and GREENBERG, B. B. Tuberculous dactylitis in the adult. *Arch. Surg.*, Jan, 1947, *54*, 67–78.

Tuberculous dactylitis or spina ventosa is usually a disease of infancy and childhood and occurs uncommonly in adults.

The authors describe in detail their experiences in a nineteen year old Negro in whom a tuberculous dactylitis was followed over a period of approximately two years following which the finger was amputated and submitted for histopathologic study.

Then follows an excellent discussion of the etiology, pathogenesis, and roentgen characteristics of tuberculous dactylitis.

According to the authors, the earliest roentgen evidence of tuberculous bone involvement in spina ventosa is elevation of the periosteum. Usually the result of an underlying serous effusion, the elevation is manifested by a linear deposit of new bone surrounding part or all of the diaphysis. Soon thereafter cortical changes may be demonstrated by an indefinite bone irregularity. Although at first swelling of the soft tissues is unusual, this soon occurs and progresses as the disease advances.

In children, the periosteal reaction is intense. The cortical expansion may be so distinct that the normal shaft may occasionally be seen within the expanded periosteal sheath of new bone. Gradually, however, the shaft is destroyed and separates as a sequestrum. The sequestrum then shows progressive fragmentation and absorption leaving a cyst-like cavity commonly called the spina ventosa. Often, however, the sequestrum may separate with necrosis of the new periosteum and fistula formation.

In adults, the initial periostitis is often replaced by a large area of rarefaction. The compact cortex becomes absorbed and the fine cancellous bone structure is replaced by much coarser cancellous patterns which often show some expansion. The bone cortex itself may be partially eroded or destroyed, with resultant sclerosis of the trabeculae in the adjacent portion of the shaft in which the cancellous bone tends to become obliterated. As the disease progresses, the cortical irregularity and sclerosis become more marked while its cancellous portion, already coarse, may develop irregular areas of rarefaction which finally appears honeycombed.

At this stage, pathologic fractures commonly develop. Finally, bone destruction may become so extensive that the debris may be seen in the perifocal soft tissues. The remaining portion of the shaft may become wide and sclerotic and the medullary cavity almost completely obliterated without the appearance of a large sequestrum, involucrum, or fistula.

The greater incidence of tuberculous dactylitis in childhood is attributed to the vascularity of these short tubular bones in the first four or five years of life. Also important is the marked regenerative power of the periosteum which is far less active in adult life.

The reproductions of the roentgenograms of the affected finger are excellent and clearly depict the progressive character of the tuberculous dactylitis in an adult from its earliest stages when only periosteal reaction was evident until marked bone destruction with a pathological fracture forced its amputation.

A fairly complete bibliography adds to the value of this review.—*Philip J. Hodes, M.D.*

BERK, MORTON E. Gout; report of an unusual case in a young man. *Am. J. M. Sc.*, March, 1948, *215*, 290–295.

Report of a case of a twenty-eight year old Filipino with proved gouty arthritis. History of onset prior to his eleventh birthday. The patient's diet was never high in purines and hyperuricemia was not present in several laboratory determinations. A tophus was found behind the ear.—*Russell R. Jauernig, M.D.*

Burrows, H. Jackson. Fatigue fractures of the fibula. *J. Bone & Joint Surg.*, May, 1948, *30B*, 266–279.

The paper consists of a review of fatigue fractures of the fibula and the author adds 5 more. The clinical and roentgen features, diagnosis, treatment and results are discussed and special note is made of the misleading freedom of ankle and tarsal movements and the occasional absence of tenderness. The fractures in the lower third occur particularly in two groups of subjects: (1) young male runners and skaters; (2) active and hard-pressed women of middle age and over. In male runners and skaters the fracture usually occurs through slender, mainly cancellous bone, 2 inches or more above the tip of the lateral malleolus; in middle-aged women the fracture is usually distal to the interosseous ligament through thicker, mainly cancellous bone, 1½ inches from the tip of the lateral malleolus. The most convenient name, Burrows suggests, is low fatigue fracture of the fibula.

His review of the literature of fatigue fracture of the uppermost third of the fibula shows that it is often precipitated by jumping. The most convenient name for it is high fatigue fracture of the fibula. Like all clinical classifications this distinction between low and high fractures has exceptions. Both high and low fractures may be bilateral.

During the first fifteen days or more no roentgen changes may be discernible. On the other hand, a fracture line may be evident after a week; sometimes none appears till the end of the second or third week. At first it is difficult to see, and even after four weeks it may be recognized only with the aid of a lens. A band of rarefaction may be seen at twelve to eighteen weeks. Callus has been observed in a child as early as the eighth day. In adults it appears during the third week, steadily consolidating and becoming organized at twelve to sixteen weeks when it forms a spindle-like thickening, crossed by a less dense stripe at the site of fracture. At forty-seven weeks it may still be just possible to distinguish thickening. A dense band is often the first indication of the fracture site and almost the last to disappear. The plane of fracture is almost horizontal; slight deviations from this are not always in the same direction so that little can be concluded about the fracturing stresses.—*R. S. Bromer, M.D.*

Rolleston, G. L., The early radiological diagnosis of ankylosing spondylitis. *Brit. J. Radiol.*, July, 1947, *20*, 288–293.

The earlier ankylosing spondylitis is recognized, the more amenable it is to treatment. The earliest appearance of the disease occurs in the sacroiliac joints, and later changes are seen at the margins of the vertebral bodies and in the costotransverse articulations.

Roentgen examinations of patients with symptoms suggesting lumbar vertebral or sacroiliac origin may be divided into four groups:

1. Anatomical abnormalities.
2. Definite pathological entities of bones or joints.
3. The frankly negative for any recognizable cause for symptoms; this group is by far the largest.
4. The borderline departures from normality. It is in this last group that the earliest changes of ankylosing spondylitis are found.

In the sacroiliac joints there is first seen loss of the normal definition of the subarticular cortex in patches. The joint margins in areas fade off into the rest of the bone. This is due to small subarticular erosions. In the superior vertebral angle of the ilium there is loss of the superficial cortical layer, producing a ragged, ill-defined edge. As the changes progress the joint margins become more irregular with a moth-eaten appearance and apparent widening of the joint space. The disease also involved the superior horizontal portion of the sacrum. As the disease progresses, there is progressive loss of the joint space, and temporary mottled calcium deposits are seen in the juxta-articular ilium and sacrum. The final stage is complete ankylosis with absorption of the sclerotic bone and relatively normal appearing cancellous bone.

In the vertebral bodies the changes may progress either up or down, and there may be involvement of the cervical and lumbar regions with initial sparing of intervening vertebrae. The earliest changes are seen in the posterior intervertebral joints, but special views are necessary to see these. In the routine films the first sign is loss of the normal convex anterior contour with sharpening of the upper and lower anterior margins. Later there is filling-in of the anterior concavity and the final stage is the development of the "bamboo spine."

The upper costotransverse joints are fre-

quently well seen in posteroanterior chest films and anteroposterior views of the cervical spine. The articular surfaces become irregular with erosions and osteoporosis. In some cases this may limit chest expansion and be one of the first signs of the disease.—*E. F. Lang, M.D.*

BARNES, ROLAND. Paraplegia in cervical spine injuries. *J. Bone & Joint Surg.*, May, 1948, *30B*, 234–244.

Twenty-two cases of paraplegia complicating injury of the cervical column are reviewed in this paper. The vertebral injury is due to flexion or hyperextension violence. Of the flexion injury, Barnes recognizes three types: (1) dislocation; (2) compression fracture of a vertebral body; (3) acute retropulsion of an intervertebral disc. He presents evidence to support the view that disc protrusion is the cause of the cord lesion when there is no roentgen evidence of bone injury, and in some cases at least when there is a compression fracture.

Two types of hyperextension injury are described: (1) dislocation; (1) injury to arthritic spines. Hyperextension injury of an arthritic spine, he considers, is the usual cause of paraplegia in patients over fifty years of age.

In one of the cases of flexion injury, the roentgenographic examination showed no evidence of bone injury. The intervertebral disc between the third and fourth cervical vertebrae was narrowed. Myelography after injection of lipiodol into the lumbar area showed complete block at the level of the herniated disc. The patient, who was examined an hour after the accident, had incomplete paralysis and sensory loss in the lower limbs, trunk and upper limbs.

Treatment of flexion injuries is discussed and Barnes presents the indications for caliper traction and laminectomy.

Elderly patients are predisposed to hyperextension injury by two factors. With advancing years there is a tendency to kyphosis of the thoracic spine which is usually compensated by a cervical lordosis, an extension deformity of the neck. This is a relatively fixed position and any increase in the degree of extension is likely to cause strain or injury. The risk of injury by hyperextension violence is greater when mobility of the spine is impaired by arthritic changes in joints and ligaments. In the event of a fall, the neck cannot be flexed in the normal defensive manner, so that when the head strikes the ground powerful angulation strain in extension is applied to the cervical region. The brunt of this violence may fall on the anterior common ligament and it may rupture, or a small flake of bone may be avulsed from the lower anterior margin of the upper vertebra. The tear extends backwards through the intervertebral disc, or the disc itself may be torn from the vertebra above. There is no tendency for the disc to herniate into the spinal canal as in flexion injuries. Once the disc has ruptured there is little resistance to further hyperextension, and considerable separation of the vertebral bodies can occur without rupture of the lax posterior common ligament or the zygapophyseal joint capsules. Immediately the striking force is removed normal alignment of the vertebrae is restored by spasm of the neck muscles and for this reason the roentgen appearances may be deceptive.

Barnes has been unable to find a completely satisfactory explanation of a spinal cord lesion in these hyperextension injuries. He suggests two possible explanations: (1) that it may be caused by "spinal concussion" as the result of minor displacement of a vertebral body; or (2) that it may be due to traction injury at the moment of extreme hyperextension.

Caliper traction is regarded as unnecessary in hyperextension injury of an arthritic cervical spine. The intervertebral disc is not displaced backward into the spinal canal and any vetebral displacement that may be present is easily corrected by moderate flexion of the neck. External splintage is not necessary and elderly patients are so intolerant of plaster jackets or collars that their application often hastens the fatal termination.—*R. S. Bromer, M.D.*

TAYLOR, ALEXANDER R., and BLACKWOOD, WILLIAM. Paraplegia in hyperextension cervical injuries with normal radiographic appearances. *J. Bone & Joint Surg.*, May, 1948. *30B*, 245–248.

A case is reported of paraplegia with normal roentgen appearances in which the cervical cord damage at autopsy was shown to have been due to hyperextension injury. In the view of the authors, the diagnosis of such cases lies between extension dislocation with immediate spontaneous reduction, and acute prolapse of an intervertebral disc. The history may clearly indicate whether the injury took place in flexion or extension. Older patients with fixed kyphotic

deformity are liable to extension injury. Disc protrusion may or may not cause spinal block, and although hyperextension dislocation does not result in continued narrowing of the spinal canal at the point of injury, yet spinal block may develop later by reason of edema of the cord due to contusion.

Roentgen examination may assist in the diagnosis by disclosing minor changes. Narrowing of a disc space, or the suspicion of wedging of a vertebra, creates a strong presumption that the compressing agent is a ruptured disc. The tearing of a small flake of bone from the anterior margin of a vertebral body suggests rupture of the anterior longitudinal ligament, and therefore extension injury. If doubt exists, myeography should dispel it, because a prolapsed disc of sufficient size to damage the cord should be visualized without difficulty.

The authors suggest that hyperextension is not the only one of the mechanisms of injury in this type of case but that it is the usual mechanism. They state that the practical value of the recognition of hyperextension injuries lies in treatment. The extended position in which, by well established usage, all cases of traumatic cervical paraplegia are treated is in fact the position most calculated to inflict further damage to the injured cord. They suggest that if the diagnosis of hyperextension injury is made, the patient should be nursed in a shell, or between sandbags, in the neutral position or even in a position of slight flexion.—*R. S. Bromer, M.D.*

Kristoff, Frederic V., and Odom, Guy L. Ruptured intervertebral disk in the cervical region. *Arch. Surg.*, March, 1947, *54*, 287–304.

The authors report 20 cases of ruptured intervertebral cervical disk. Their experiences have led them to believe that there are three successive stages in the pathogenesis of ruptured cervical disks. The first period is that of root compression. The second period is that of unilateral cord compression with or without masked root compression. The final or third period is that of bilateral cord compression with masked unilateral or bilateral root compression.

The authors believe the diagnosis of cervical disc lesions is primarily clinical and that the history and subjective complaints are of the greatest assistance in early diagnosis. Considerable emphasis is placed upon the diagnostic significance of being able to reproduce the pain and paresthesias complained of by the patient by manipulation of the lower cervical spine.

In the cervical canal, there is a much closer relationship between the cervical interspaces and their corresponding nerve roots. Because of this, root compression in the cervical canal is localized with much greater accuracy than in the lumbar spine. Of importance, too, is the fact that in the cervical canal, the spinal cord is anchored on both sides by the dentate ligament which tends to fix the cervical neural structures thereby accounting for the rapidity of onset of signs and symptoms in relatively small protrusions of the disk.

Ruptured disks at the 5th cervical interspace produce pain and paresthesias in the radial side of the arm, thumb and index finger. Sensory impairment, if present, may involve the same area. There may be associated weakness of the deltoid and biceps muscles.

Ruptures at the 6th cervical interspace are attended by pain and paresthesias referable to the extensor side of the arm, dorsum of the hand and one or all of the three middle fingers. Sensory impairment, if present, may involve the same area or part thereof. Weakness primarily involves the triceps muscle.

Roentgenograms of the cervical spine are of questionable value in these lesions. In some instances, the physiological cervical lordotic curve may be absent. Oblique views of the cervical spine may or may not show localized arthritic changes and narrowing of the intervertebral foramina.

The authors re-emphasize the fact that apparently normal roentgenograms of the cervical spine are not uncommon in patients with proved ruptured cervical intervertebral disks.

The importance of myelography and the accuracy of the method is re-emphasized.

The authors divide their discussion into two sections depending upon whether the lateral intervertebral disk protrusions with root compression are complicated by or are uncomplicated by cord compression.—*Philip J. Hodes, M.D.*

Peyton, William T., and Simmons, Donald R. Herniated intervertebral disk. *Arch. Surg.*, Sept., 1947, *55*, 271–287.

The authors report their experiences in 90 patients operated upon for herniated interver-

tebral disks. In 10, the intervertebral disk was considered normal at operation. In 80 patients, the intervertebral disk was considered abnormal. To be considered abnormal or pathologic, a portion of the disk had to lie loose as a fragment of tissue in the spinal canal or had to protrude spontaneously when the annulus fibrosus was opened.

The results were considered satisfactory in most of the patients in whom a definitely pathologic disk was found and removed. Seventy-two of the 80 patients in this latter group were followed and in only 3 was continued pain or disability reported. The results were uniformly unsatisfactory in the 10 patients in whom a normal intervertebral disk was found.

During the authors' early experience spinal fusions were not performed after the disk was removed. More recently, however, routine spinal fusions accompanied every disk operation. The results indicated that when truly pathologic intervertebral disks were operated upon, it made little difference whether or not the removal of the intervertebral disk was accompanied by spinal fusion.

Routine roentgenograms of the lumbosacral portion of the spine seemed to indicate that bony abnormalities were not predisposing causes of herniation of intervertebral disks in the present series. Of the 90 patients examined roentgenographically, in 16 narrowing of the interspace involved by the pathologic disks was reported. Of equal significance, however, was the occurrence of similar narrowing at levels other than the one involved by the pathologic disk.

Discussing contrast studies of the spinal canal, the authors report that they discarded air myelography in 1941 because they thought the procedure was unreliable. Since then, they have used radiopaque substances (pantopaque) in selected cases only. Many patients with classical symptoms were not examined in this manner since operation would have been performed even though the myelograms proved to be negative. In other patients in whom the findings were less definite, the contrast study of the spinal canal was carried out in the hope of obtaining additional evidence.

Contrast myelograms were obtained in 46 of the 90 patients operated upon. A correct diagnosis was made in 41 instances. In 3, the roentgen diagnosis was wrong.—*Philip J. Hodes, M.D.*

CLEVELAND, MATHER, BOSWORTH, DAVID M., and THOMPSON, FREDERICK R. Pseudarthrosis in the lumbosacral spine. *J. Bone & Joint Surg.*, April 1948, *30A*, 302–312.

The paper is divided into two parts: first, the incidence of pseudarthrosis in fusion of the lumbosacral spine; and second, statistics regarding the repair of pseudarthrosis. Among 594 patients, 1,329 spinal intervals were bridged. Pseudarthrosis developed in 161 intervals among these patients, or 12.1 per cent. Among the 594 patients, 119 developed pseudarthrosis, or 20 per cent. It was found that the percentage of pseudarthrosis rose rapidly as the number of spinal intervals, which were crossed, increased.

Failure of fusion was demonstrated much more frequently when roentgenograms of front and side bending (biplane) were superimposed than by use of flat roentgenograms and clinical observation. In these biplane roentgenograms, the lateral flexion and extension films should show the fused elements completely superimposed. In the superimposed anteroposterior lateral-bending roentgenograms, the fused elements appear as if stereoscoped, but the borders of the bodies of the spinous and transverse processes are parallel. The use of such superimposed roentgenograms has increased the known percentage of pseudarthrosis, when tabulated both as to clinical incidence and true incidence. In the study of the authors' cases no result was accepted as regards solidity of fusion with less than one year of follow-up, unless controlled by both lateral roentgenograms in flexion and extension and by anteroposterior roentgenograms in right and left bending.

Of the 119 patients in whom pseudarthrosis developed, only 35 returned to the authors for repair. Many of the remainder had symptoms sufficient for repair. These cases are analyzed in detail in the paper. Relation of the failure of pseudarthrosis repair to the type of operation and causes for the development pseudarthrosis are also discussed.—*R. S. Bromer, M.D.*

HORWITZ, THOMAS. The treatment of congenital (or developmental) coxa vara. *Surg., Gynec. & Obst.*, July, 1948, *87*, 71–75.

This investigation is based on 17 cases of congenital or developmental coxa vara. This deformity should be suspected in any child who manifests a painless limp. Pain which appears in adolescence and in the adult is depend-

ent on the degree of deformity and shortening and upon the extent of degenerative changes which affect the hip joint (largely on a static basis). The roentgenograms and histologic studies in these cases show a pronounced disorganization of the femoral neck in the region of, and distal to, the epiphyseal plate. The exact nature of these changes is not clearly understood.

An evaluation of the results of surgery in these 17 cases of coxa vara fails to justify the use of drilling of, or introduction of a bone graft through, the femoral neck as a procedure supplemental to corrective osteotomy. The results have been satisfactory more consistently, with a lesser incidence of immediate postoperative complications, following simple subtrochanteric osteotomy than by any other method. Recurrence of coxa vara deformity after subtrochanteric or intertrochanteric osteotomy in 4 cases was due to mechanical difficulties. These difficulties involved the control of the postosteotomy fragments in the presence of a movable hip joint.—*Mary Frances Vastine, M.D*

Bost, Frederic C., Hagey, Helen, Schottstaedt, Edwin R., and Larsen, Loren J. The results of treatment of congenital dislocation of the hip in infancy. *J. Bone & Joint Surg.*, April, 1948, *30A*, 454–468.

This paper is a study of the results of treatment of congenital dysplasia and of congenital dislocation of the hip in 112 such disorders which occurred in 86 patients, upon whom treatment was commenced in the first three years of life. The report is actually a study of the early results, covering a period of from one to thirteen years after the commencement of treatment. The types of disorders follow the suggestion of Hart, being designated as either dysplasia or as dislocation of the hip. The first term is applied to those hips which lack normal development of the roof of the acetabulum, and the second designates those hips in which dysplasia was found in conjunction with some outward or upward displacement of the head of the femur. No case of arthrogryposis was included in the series.

The authors regard roentgenography as the sole means by which the anatomical condition of the hip may be judged. The interpretation of the roentgenogram should include specific information concerning both the acetabulum and the head and neck of the femur, as well as their relation to one another. The measurements of Hilgenreiner were used as they satisfy these requirements. In this measurement the transverse or Y line extends between the tips of the ilia at the region of the triradiate cartilage. The slope of the acetabulum is measured from the tip of the ilium to the upper and outer portion of the acetabulum. The angle between the line marking the roof of the acetabulum and the Y line has been designated as the "acetabular index." A third line, drawn perpendicular from the Y line to the highest point of the upper femoral diaphysis, permits the measurement of the distance of the femoral diaphysis either upward or downward from the Y line, and also its distance outward from the tip of the ilium at the base of the acetabulum. The measurement of Perkins, which is a perpendicular line from the upper and outer border of the acetabulum to the Y line, is helpful in indicating the position of the head of the femur. The Y coordinate for the hip joint is the measurement from the line of gravity of the body, as represented by a longitudinal line through the mid-sacrum, to the center of the head of the femur.

If comparisons of roentgenograms are made, a standard technique must be used and the roentgen tube must be well centered over the pelvis which has been placed in a symmetrical position with the knees together and the patellae uppermost. When any doubt exists concerning the hip joint, the roentgenograms should be repeated at intervals. While the mathematical accuracy of the interpretation of the roentgenograms may be open to question, nevertheless the comparison of the two hips and of roentgenograms taken in series provides relative accuracy upon which judgment may be based.

Excellent or nearly excellent anatomical results were obtained in 55.4 per cent of the cases. Good anatomical results were produced by treatment in infancy in 81.3 per cent, and good functional results in 80.4 per cent of the hips examined. Development of the acetabulum progressed slowly, indicating a probable need for longer periods of fixation after reduction of the hip. Delay in reduction of dislocation was found to cause increasing maldevelopment of the hip, due in part to a thickening of the acetabular floor coincident with an increase in the Y coordinate. There was found, also, a direct relation between the early institution of treatment and the good results reported.—*R. S. Bromer, M.D.*

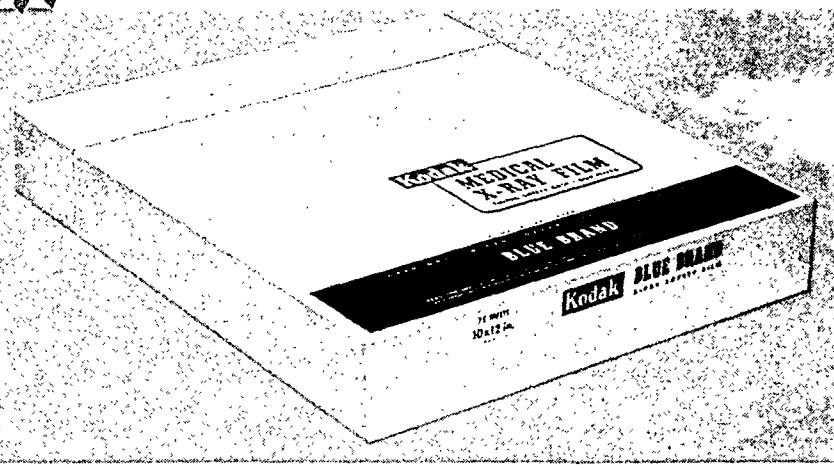
DONALDSON, S. W., BADGLEY, CARL E., and HUNSBERGER, W. G. Lateral view of the pelvis in examination for hip dislocation. *J. Bone & Joint Surg.*, April, 1948, *30A*, 512–514.

A technique is recommended for lateral view of the pelvis in examination for dislocation of the hip. Stereoscopic anteroposterior views of the pelvis and both hip joints do not always give complete information to determine the exact amount of displacement. The technique employed and the position of the patient for such a roentgenogram are the same as used for the lateral view in pelvic measurement examination, fractures of the sacrum and lesions of the lower lumbar spine and the lumbosacral disc. Routine roentgenograms of the pelvis and both hips are first made; and, if they show extensive fractures of the pelvis, then the lateral view is omitted for obvious reasons. If the roentgenograms reveal only a dislocation of the femoral head, or a dislocation with an acetabular fracture, the patient is placed in the proper position on the Bucky table for a lateral projection of the pelvis. Sometimes it is more comfortable for the patient to lie with the injured hip on the table top instead of away from it. The additional exposure not only shows the amount of displacement of the head of the femur, but also shows the position of any small bony fragments if present, either inside or outside of the joint capsule. Such a roentgenogram is also of value in the check-up examination following manipulation for reduction of a simple dislocation without fracture. The authors found that examinations with a portable apparatus, while the patient is in bed and extension applied, have not been satisfactory, either with or without a stationary grid.—*R. S. Bromer, M.D.*

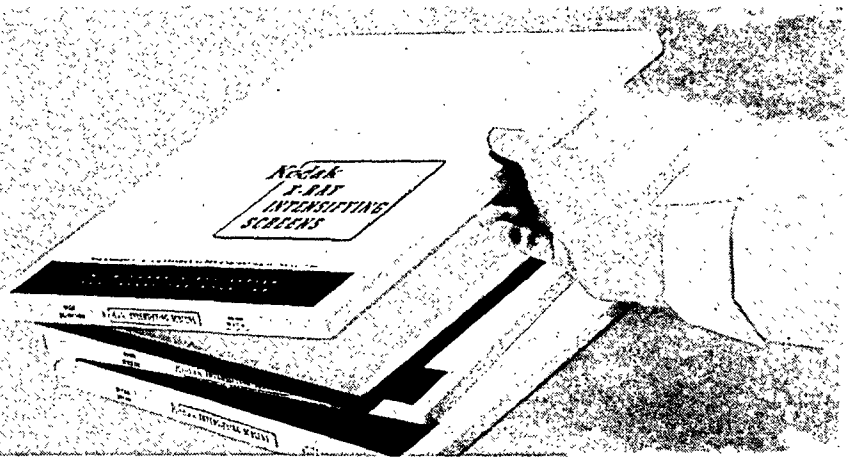
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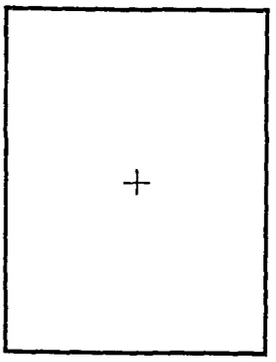
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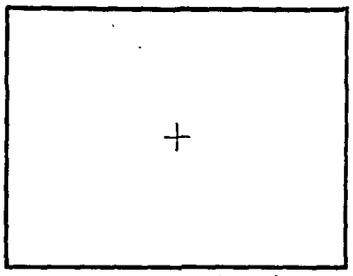
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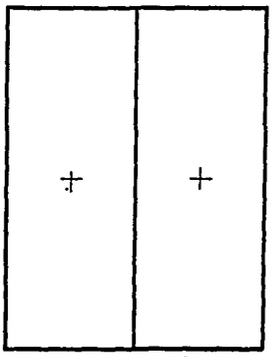
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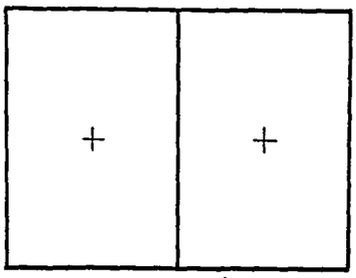
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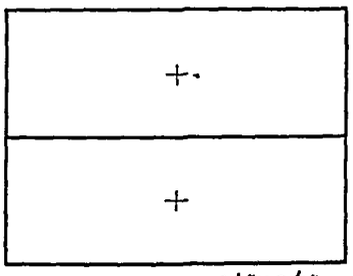
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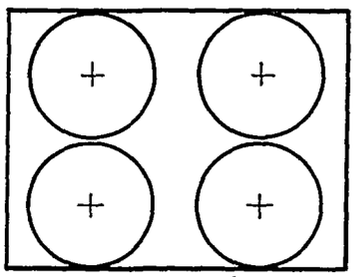
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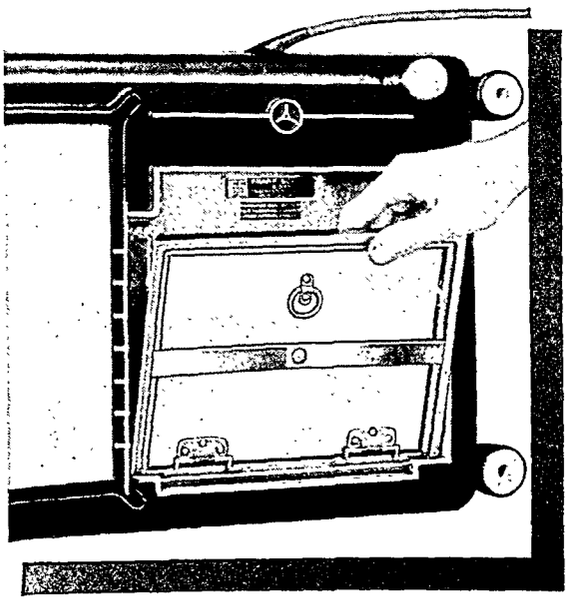
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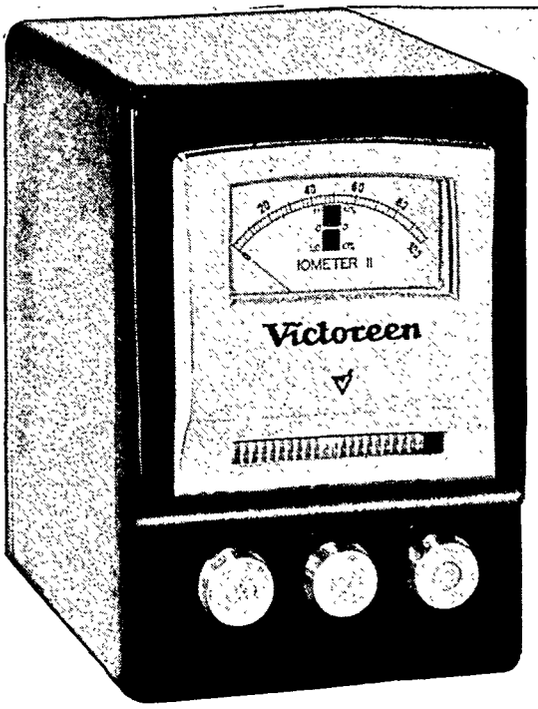
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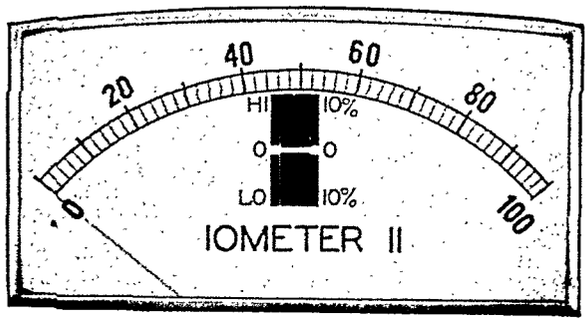
The Victoreen Iometer II is used as a constancy meter which when set to a desired x-ray beam intensity will indicate the percentage deviation from the predetermined setting. An ionization chamber is mounted permanently in the master cone or x-ray tube housing.

The Iometer II is furnished in a case equally adaptable for mounting on a vertical control panel or on a desk. It is inherently stable. The chamber may be placed sufficiently below the filters to eliminate the possibility of temperature error or secondary radiation from the filters.

The Iometer follows closely the values of the beam as read by an r-meter and the same laws of temperature and pressure apply. The absorption of the ionization chamber is very low so that the Iometer may be used on superficial as well as deep therapy equipment.

The new Iometer II incorporates the best features of a null type system. It requires no matching of tubes—the tubes are not used as part of the calibrated circuit—it covers a wide range of intensity values with equal accuracy and with an r-meter assures protection and almost perfect dose control.

For practicability and convenience two scales are incorporated on one meter face. One scale arbitrarily calibrated from 0-100 provides the pre-treatment setting, the other 10-0-10 indicates the percentage change in beam intensity during treatment. The meter is illustrated below.



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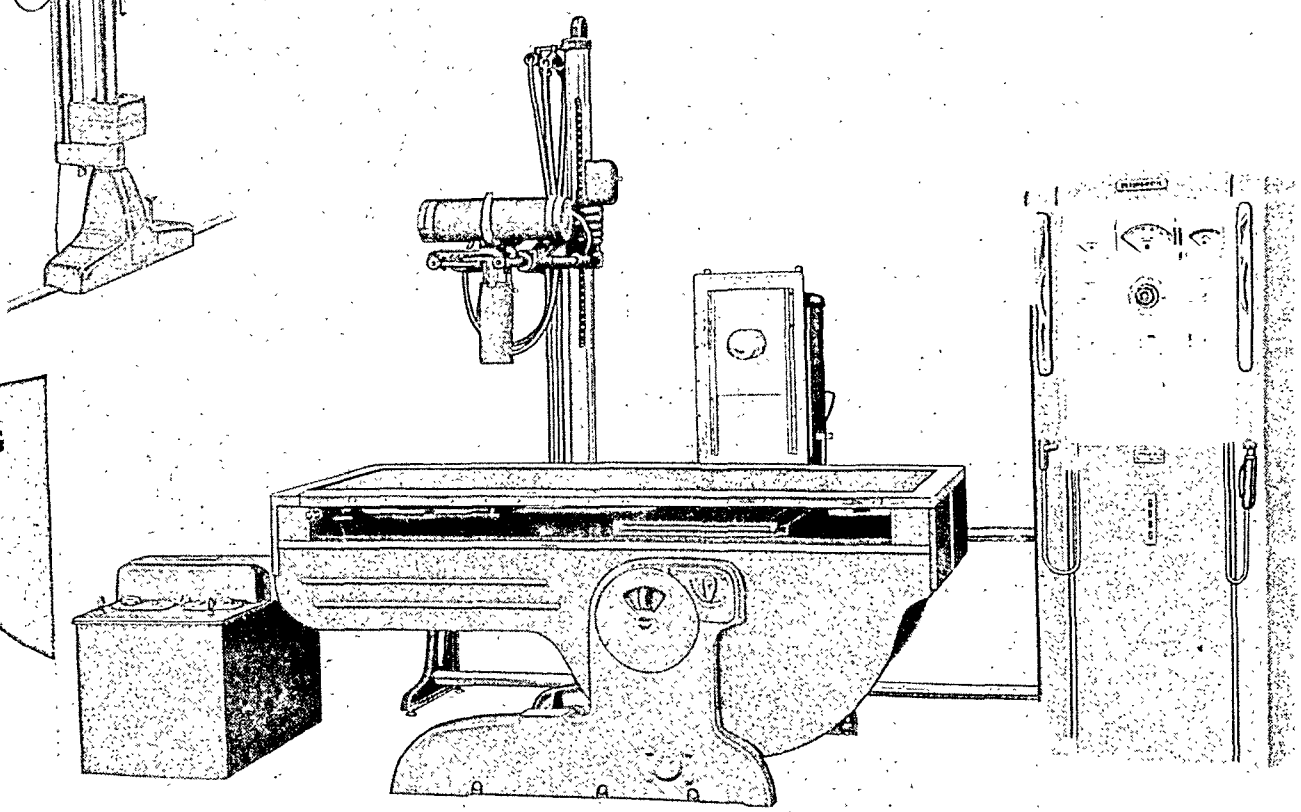
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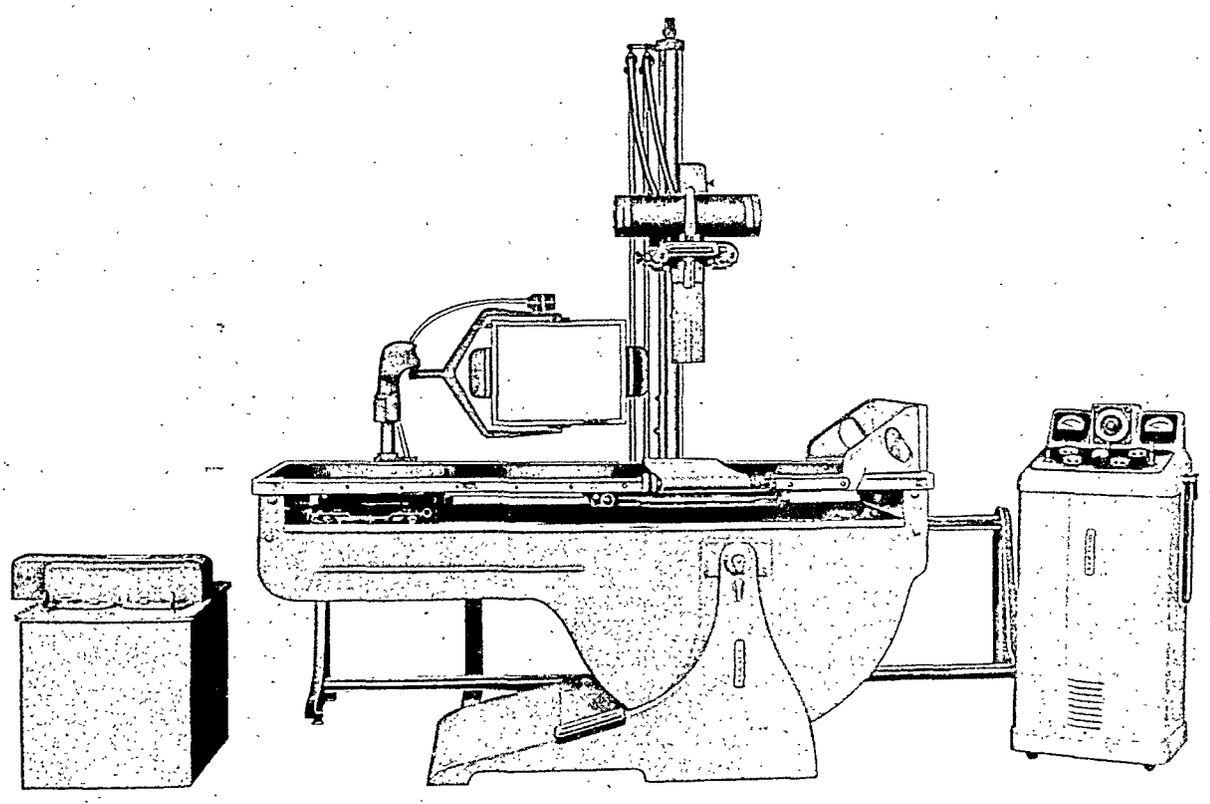
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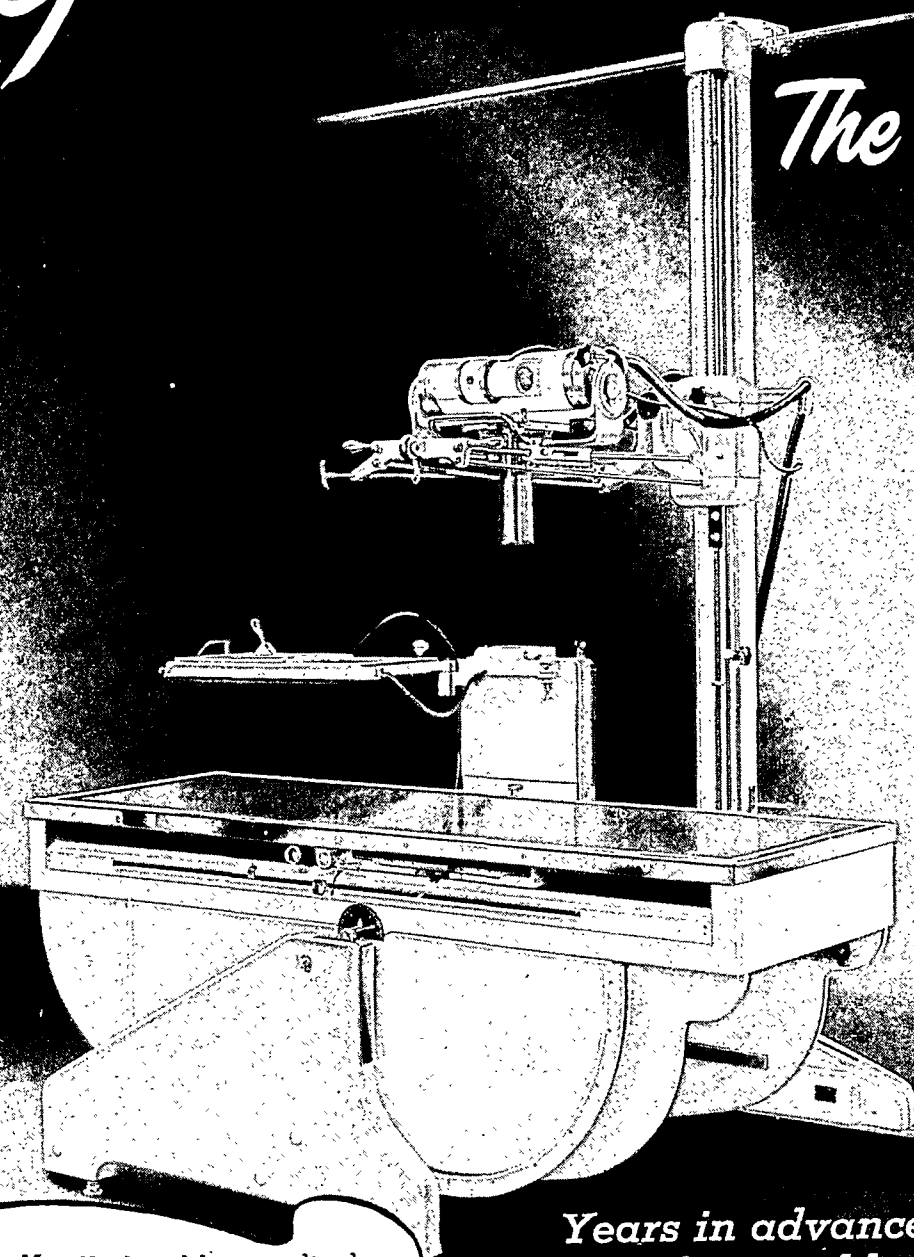
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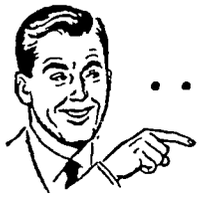
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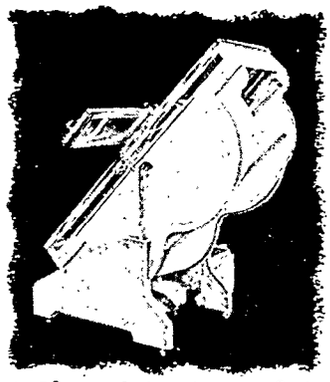
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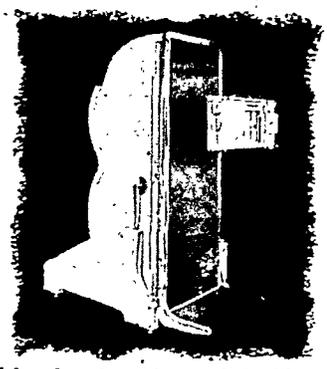


...WITH 45° TRUE TRENDELENBURG

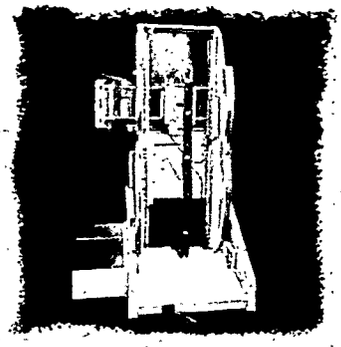
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10. Double sets of limit switches control table travel.
11. Motor housing serves as observation platform.
12. Table is driven from both sides by double gear segment.
13. 135° of angulation . . . from 45° Trendelenburg through horizontal to vertical.
14. X-Ray absorption maximum of 0.5 MM of Aluminum at 60 PKV.
15. Table is impervious to water and diagnostic solutions.
16. No holes in table top . . . attachments are made on side of table.
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18. Bucky covers up to 66" of table range . . . to within 3" of foot end.
19. Reciprocating Bucky available.
20. For Fluoroscopic work, uses Patterson B-2 screen and Scholz four and one spot film tunnel.
21. Fluoroscopic tower is disappearing type.
22. Fluoroscopic screen or spot film device has four positive locks for every technic.
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24. 18" focal spot without reduction of table angulation.
25. Interchange of tubes easily done in field.
26. Lead bronze cone and steel plate protect against scattered radiation.
27. Cross travel of fluoroscopic tube is 10", longitudinal—42"
28. Fluoroscopic screen moves up to 66" above floor (vertical).
29. Cables and wires arranged for freedom of movement.



135° angulation from 45° Trendelenburg through horizontal to vertical.



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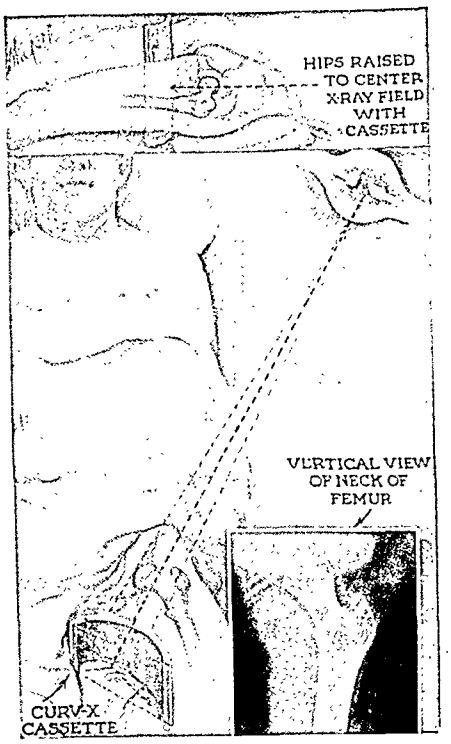


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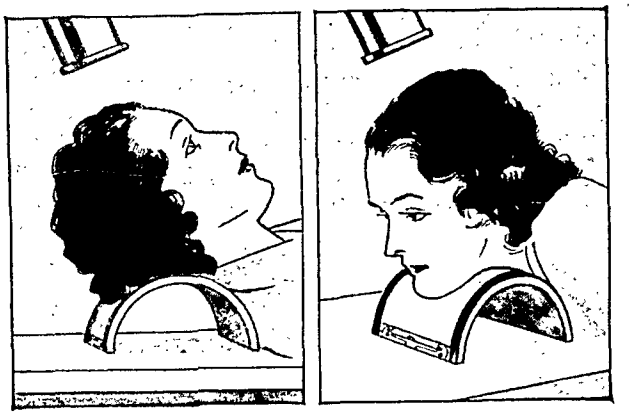
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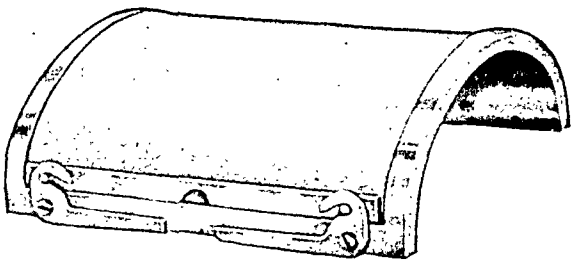


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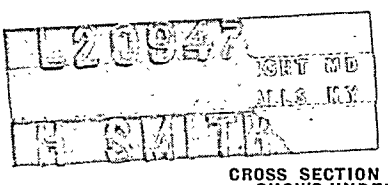
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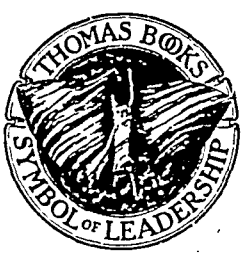
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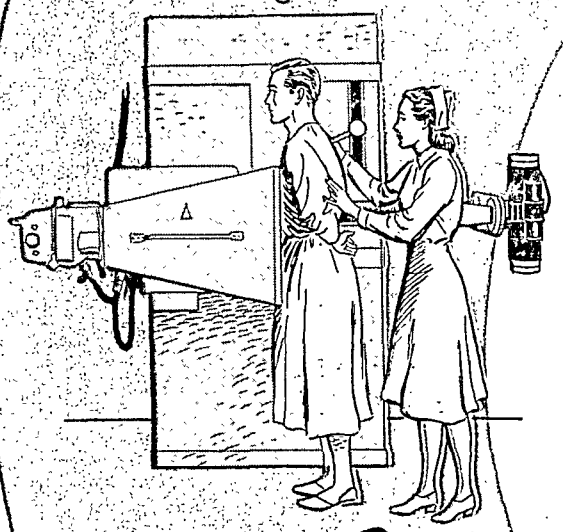


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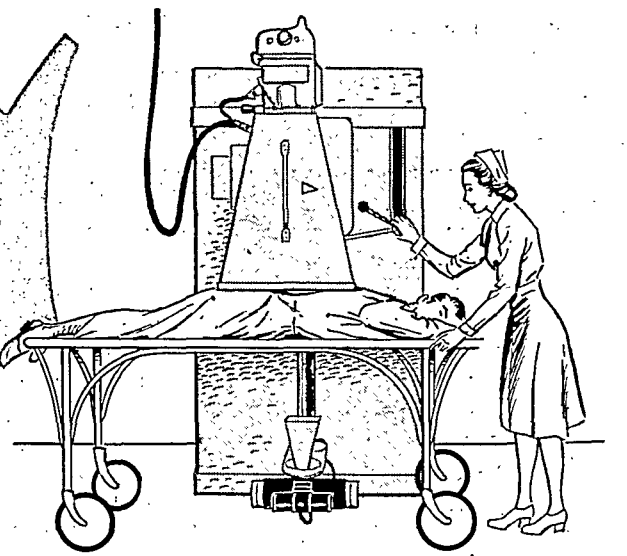
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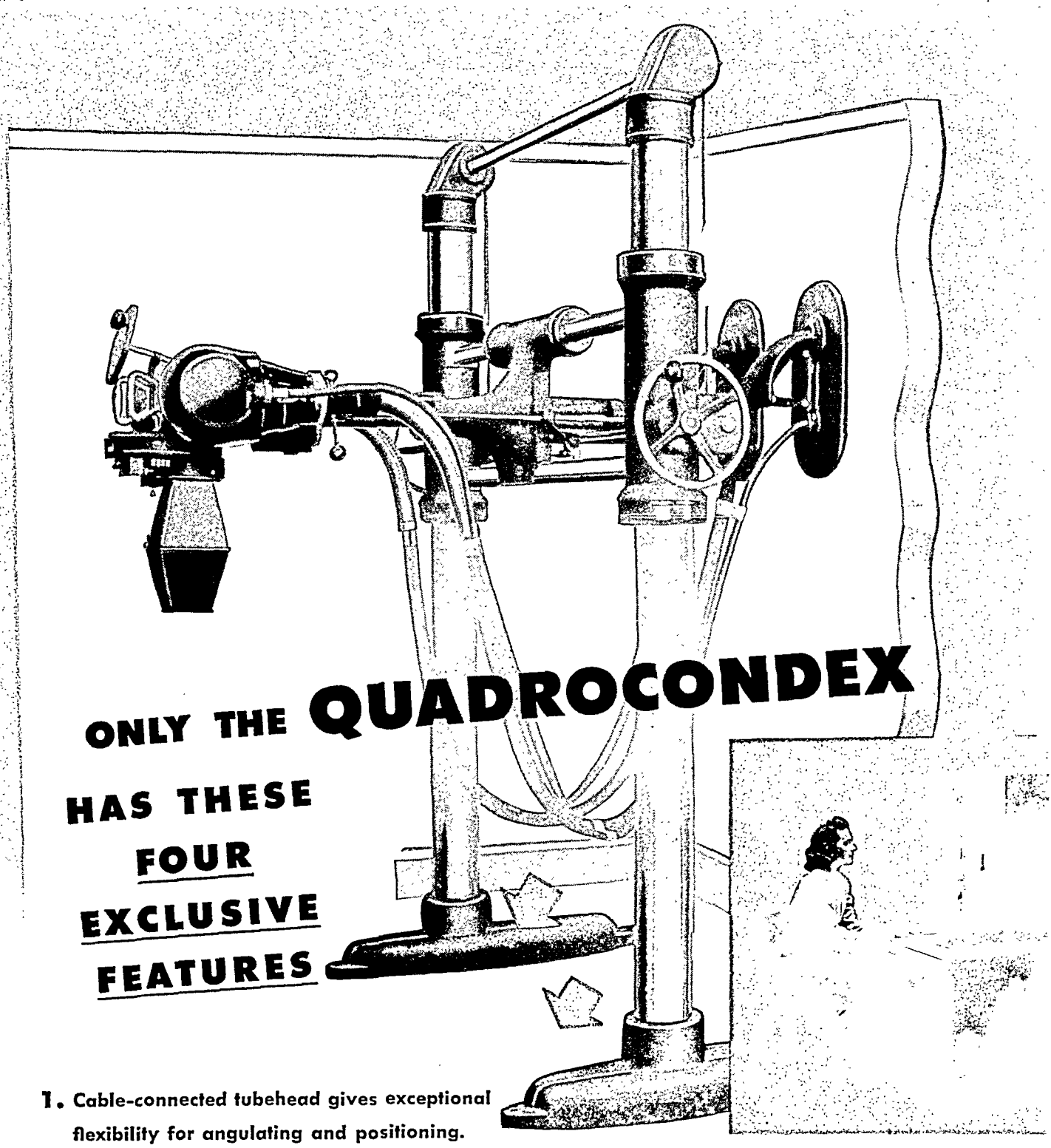
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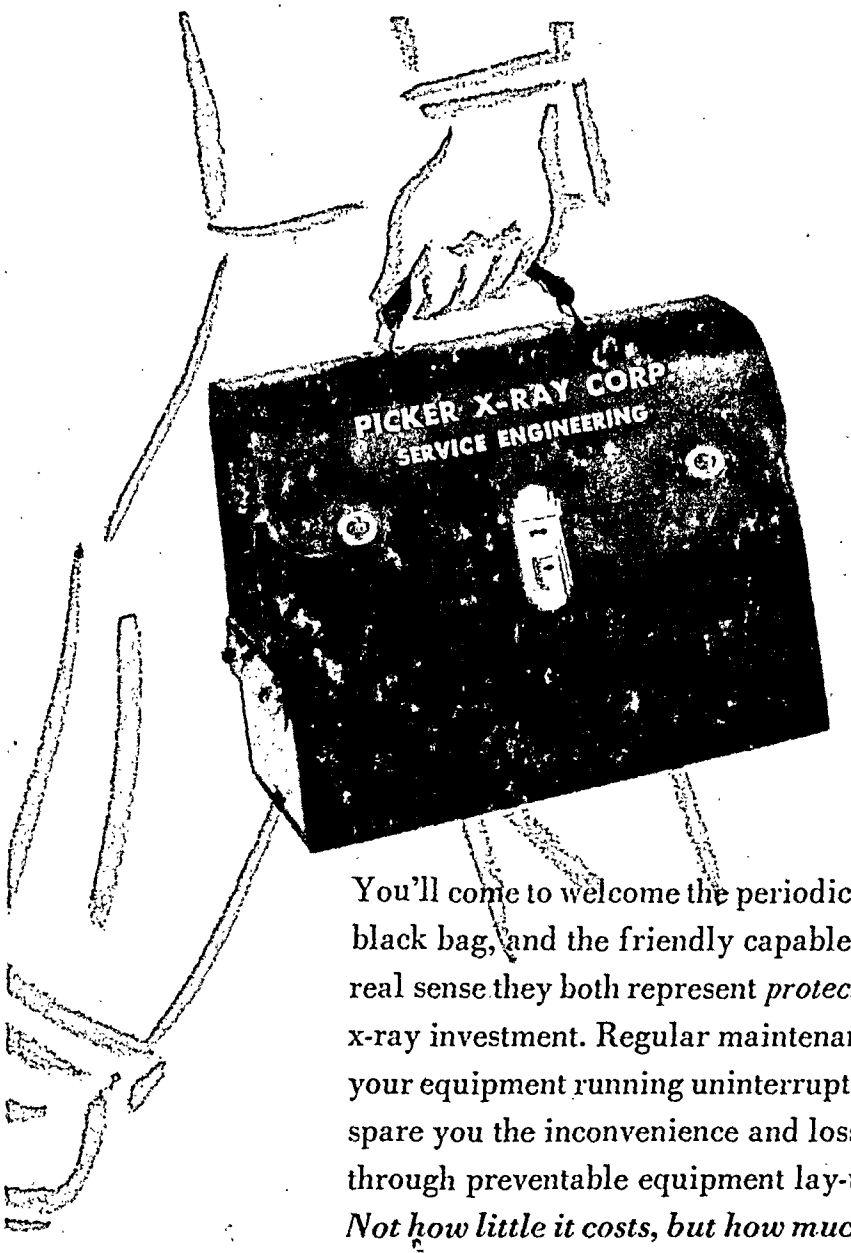
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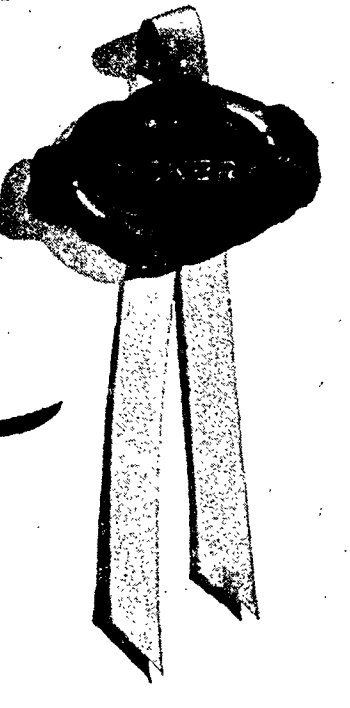
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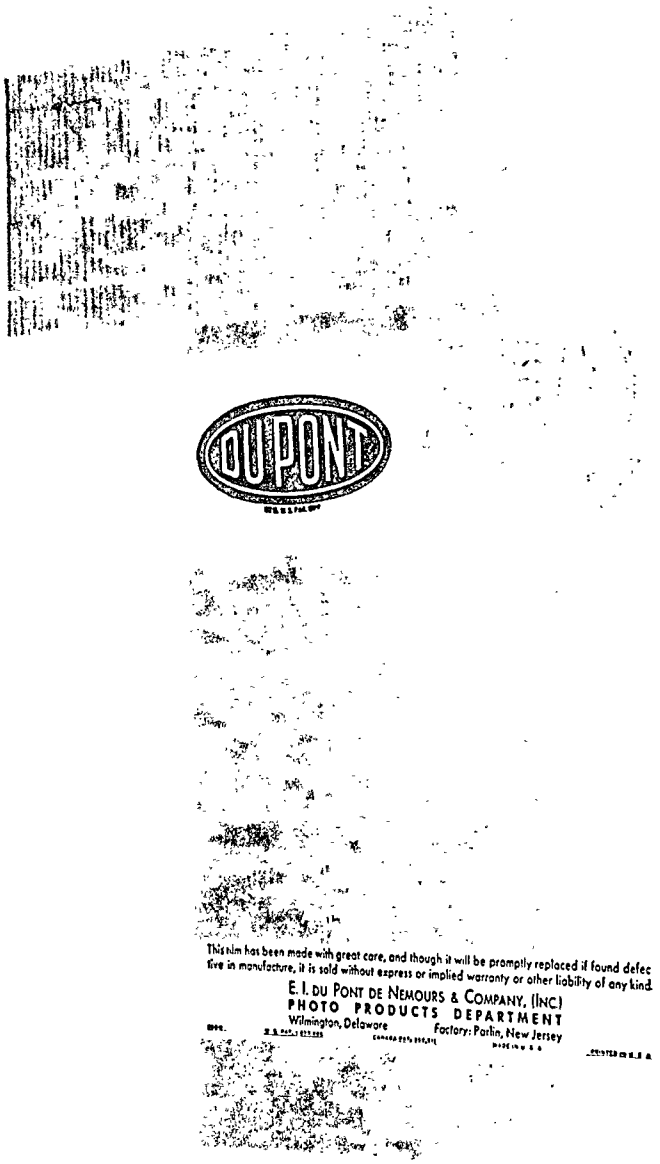
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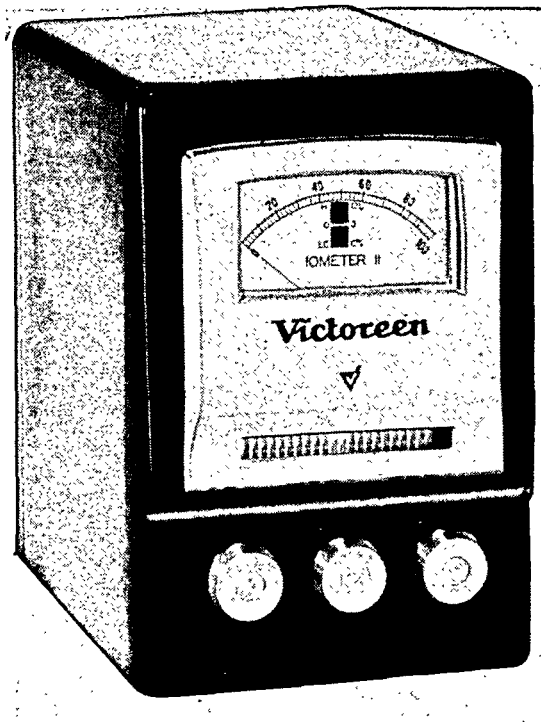
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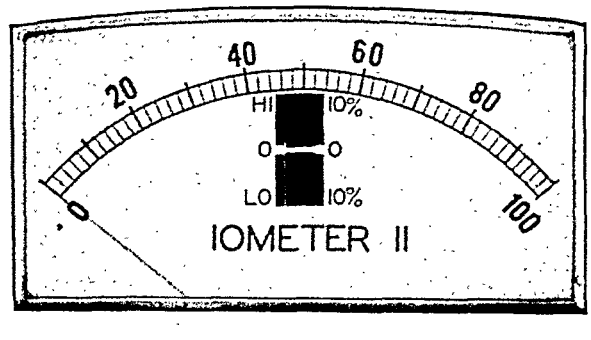
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CONTENTS

Some Medical and Roentgenological Aspects of Mass Chest Surveys ARTHUR C. CHRISTIE, M.D. 147

The Value of Roentgenology in the Prognosis of Minimal Tuberculosis ARCHIBALD L. COCHRANE, HAROLD W. CAMPBELL, AND SAMUEL C. STEIN 153

Vertebral Angiography . . . OSCAR SUGAR, LAWRENCE B. HOLDEN, AND CHESTER B. POWELL 166

The Detection of Gastric Carcinoma by Photofluorographic Methods. Part I. Introduction JOHN F. ROACH, ROBERT D. SLOAN, AND RUSSELL H. MORGAN 183

The Detection of Gastric Carcinoma by Photofluorographic Methods. Part II. Equipment Design . . . JOHN F. ROACH, ROBERT D. SLOAN, AND RUSSELL H. MORGAN 188

The Azygos Lobe: Its Involvement in Pulmonary Disease EMIL ROTHSTEIN, M.D. 195

Occurrence and Diagnosis of Dilatation of the Aorta Distal to the Area of Coarctation FELIX G. FLEISCHNER, M.D. 199

Left Atrial Calcification in Rheumatic Heart Disease BERNARD S. EPSTEIN, M.D. 202

A Case of Bronchial Adenoma without Signs of Bronchial Obstruction, Concomitant with Minimal Pulmonary Tuberculosis CAPTAIN GILBERT H. FLETCHER, M.C., AND MARION S. LOMBARD 209

Intraluminal Diverticulum and Other Lesions Producing Intermittent Duodenal Obstruction or Stasis RICHARD E. KINZER, M.D. 212

The Roentgen Manifestations of Pancreatitis Complicating Mumps M. H. POPPEL, M.D., F.A.C.R., AND CELIA BERCOW, M.D. 219

Demonstration of Sinus Tracts, Fistulas and Infected Cavities by Lipiodol MAJOR JAMES M. DELL, JR., M.C. 223

Principles of Fast Electron Therapy in Cancer ERICH M. UHLMANN, M.D., F.A.C.R., AND LESTER S. SKAGGS, Ph.D. 232

Part Time Radiological Practice in Hospitals of Small Cities WILLIS S. PECK, M.D. 236

Department of Technique

Contribution to the Technique of Bronchography in Adults L. WALK 243

Malleable Cones for Roentgen Therapy ROBERT S. LEIGHTON, M.D. 245

Editorials

Legg-Perthes' Disease RALPH S. BROMER, M.D. 248

Hirschsprung's Disease 250

William Gregory Cole, 1902–1948 . . . RAMSAY SPILLMAN, M.D. 252

Society Proceedings, Correspondence and News Items 254

Abstracts of Roentgen and Radium Literature 261

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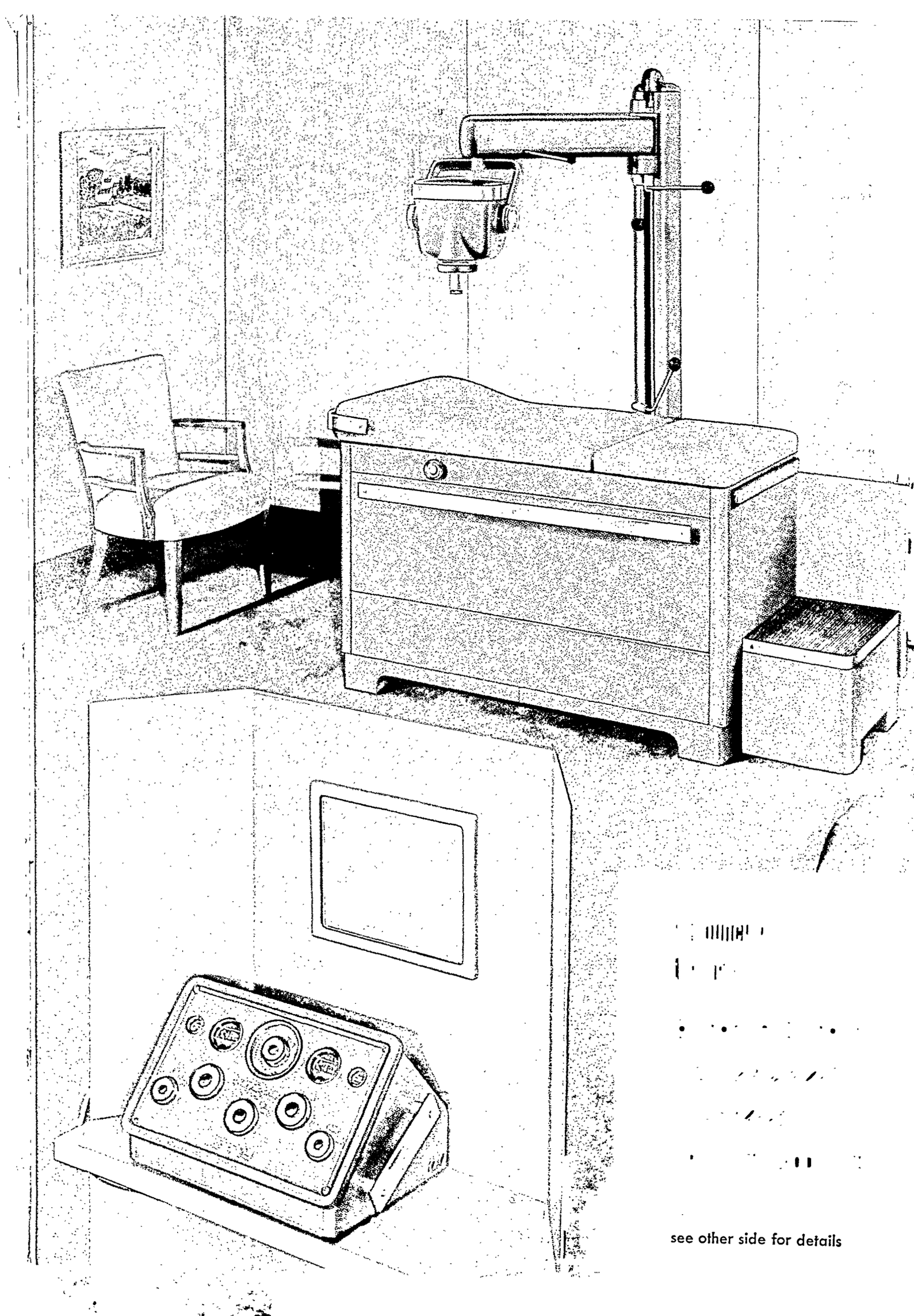
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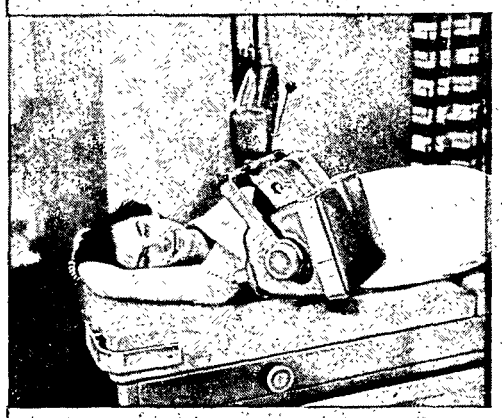
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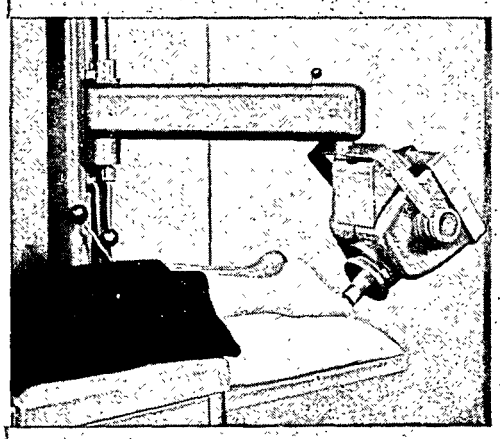
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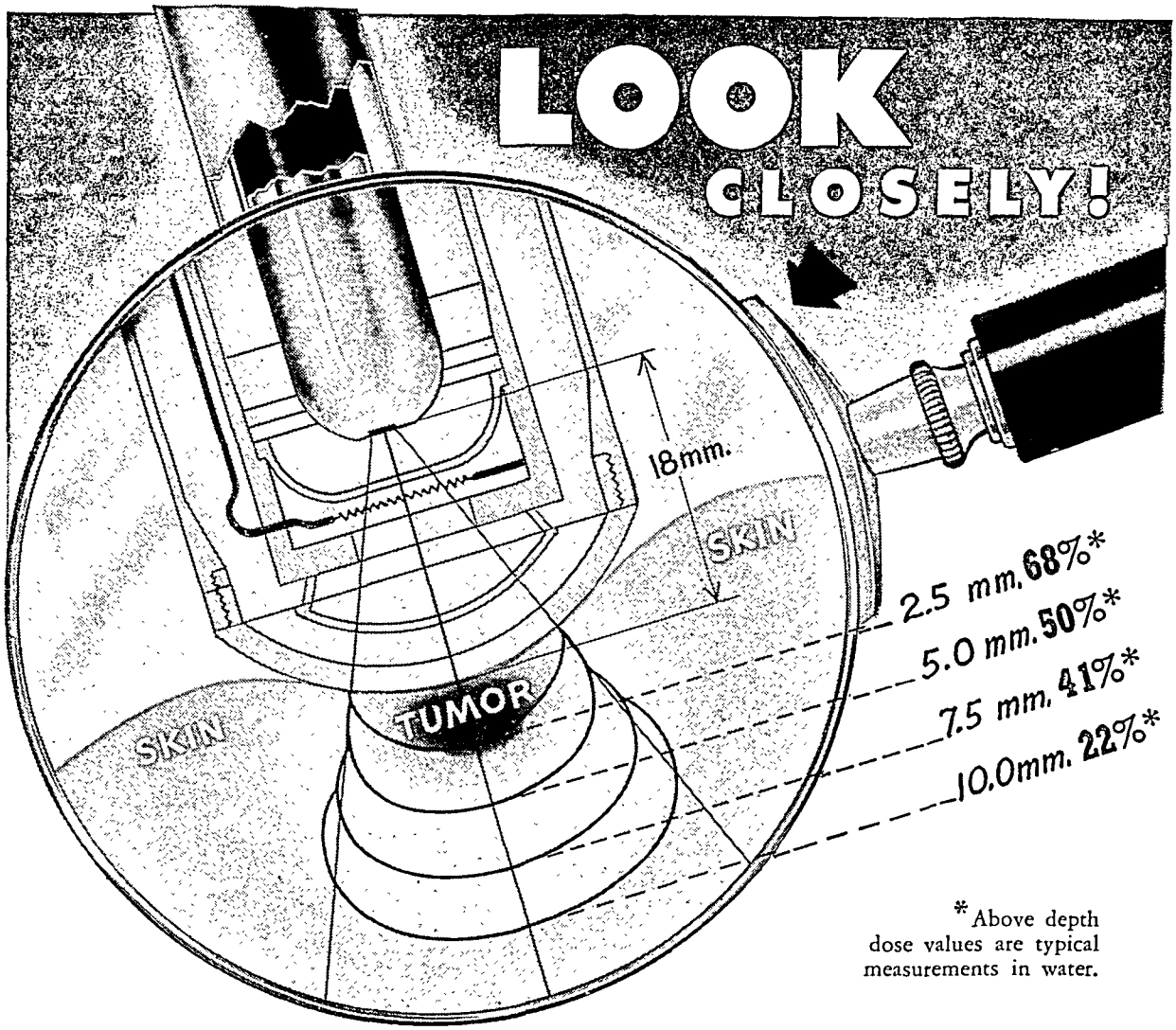
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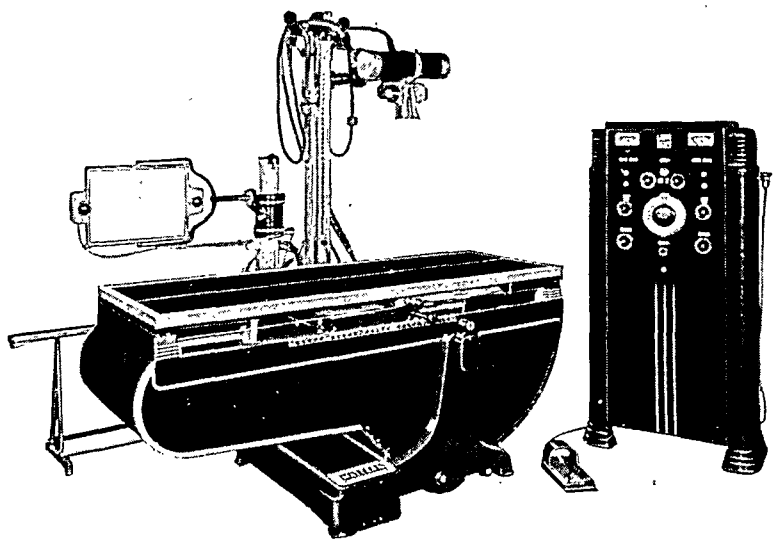
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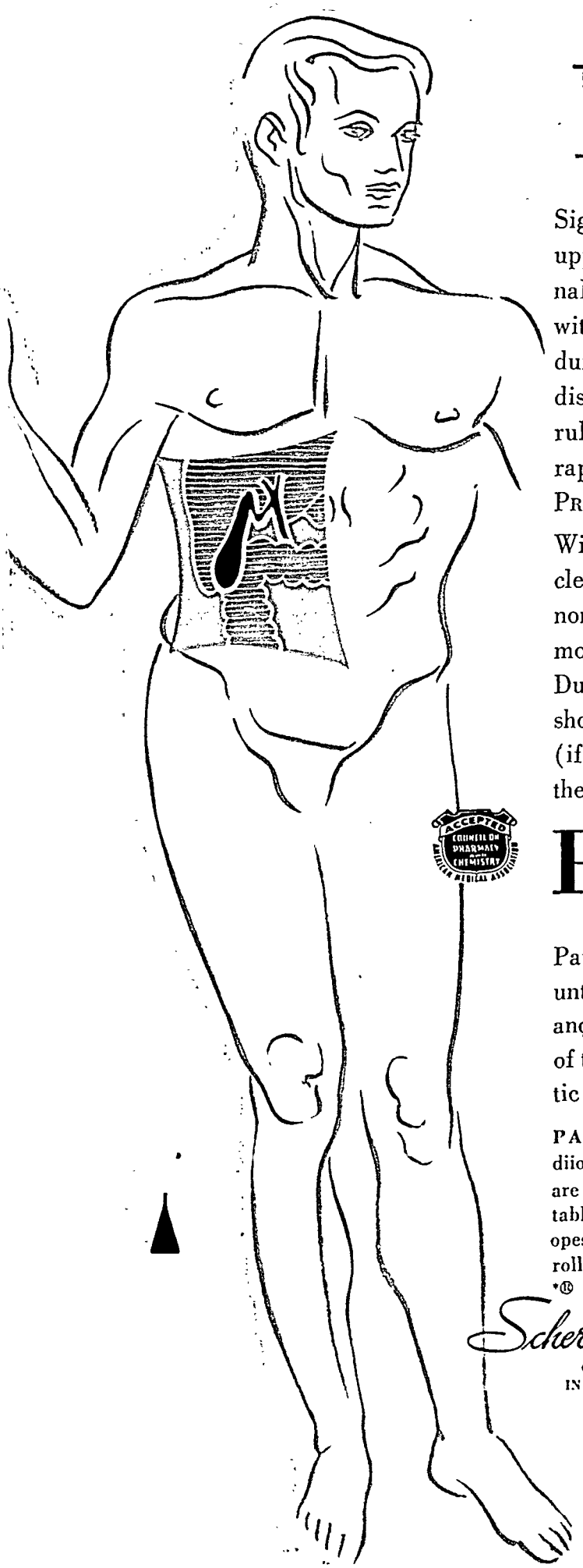
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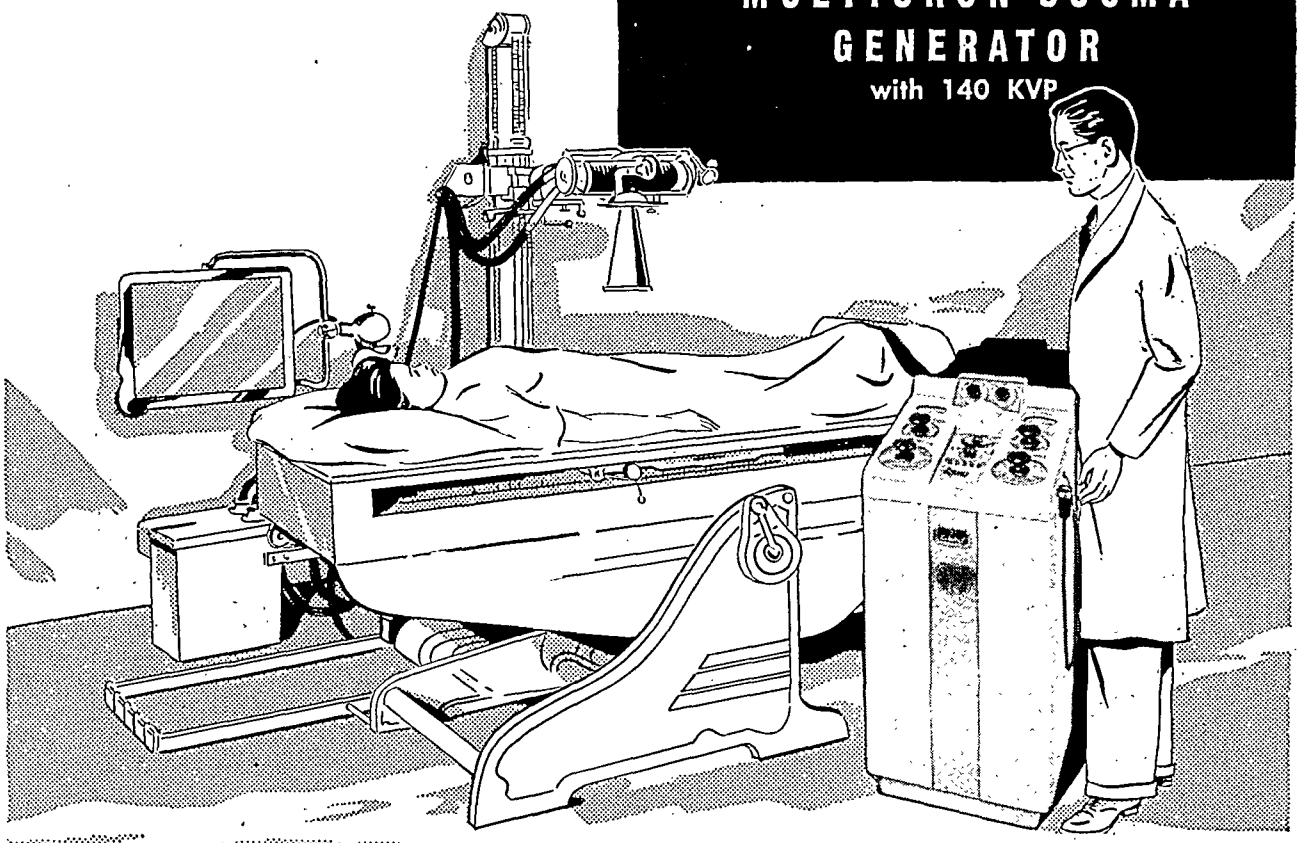
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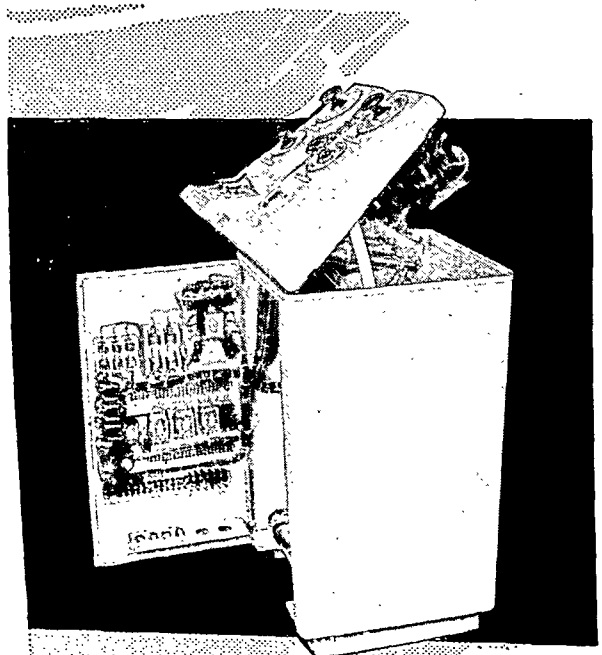
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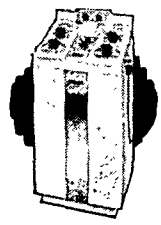




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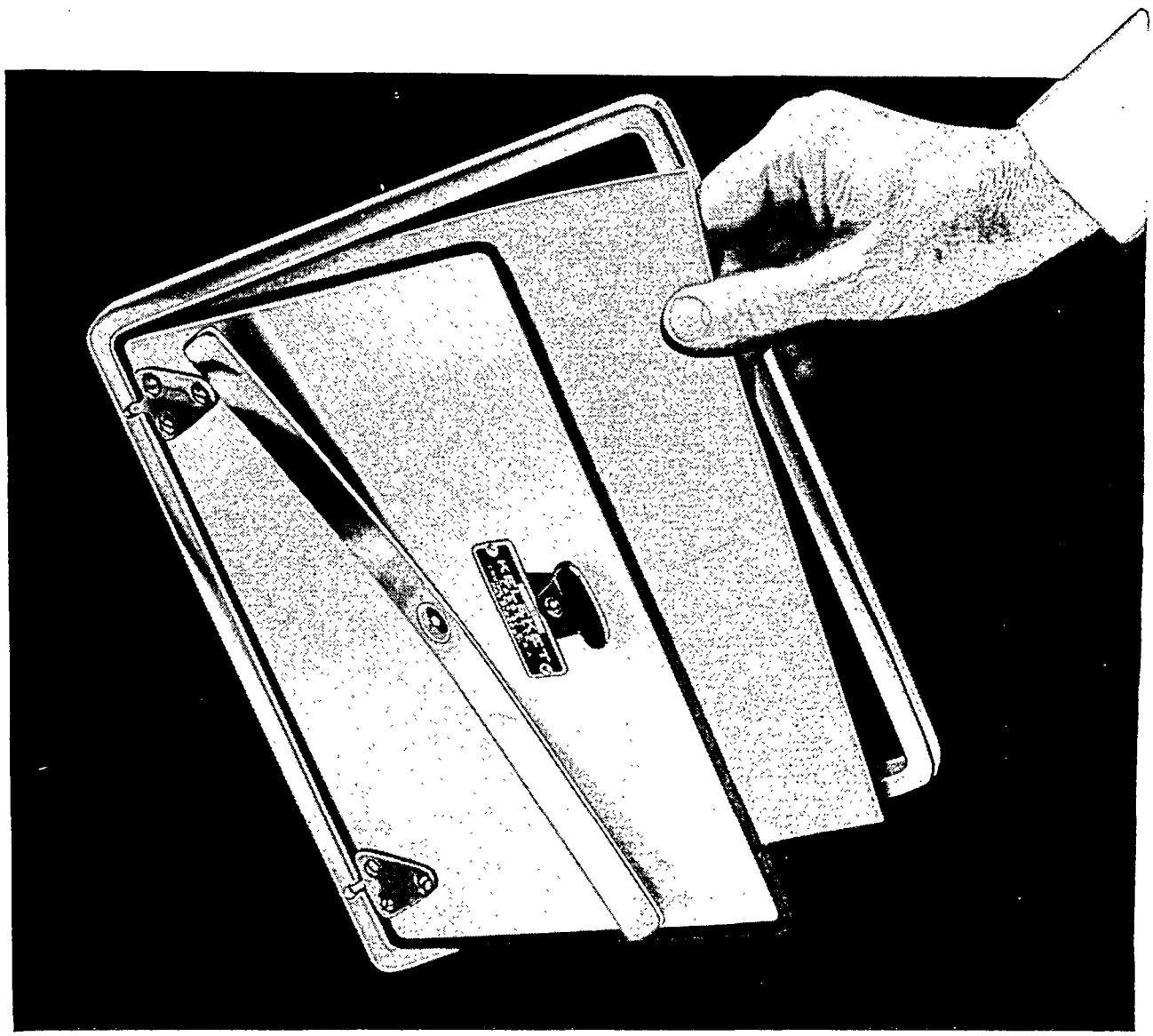
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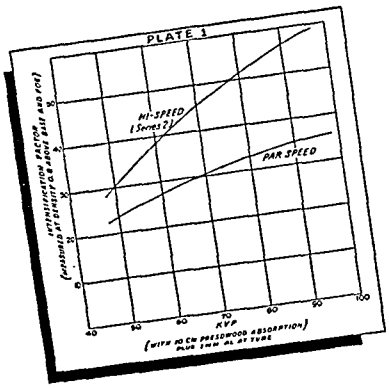


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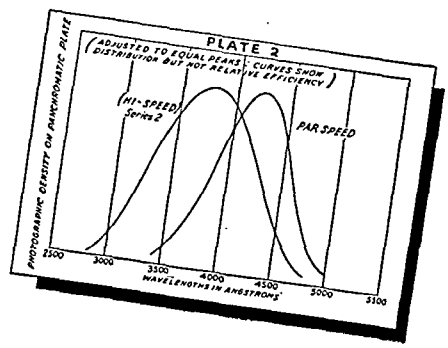


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VOL. 61 FEBRUARY, 1949 NO. 2

SOME MEDICAL AND ROENTGENOLOGICAL ASPECTS OF MASS CHEST SURVEYS*

By ARTHUR C. CHRISTIE, M.D.

WASHINGTON, D. C.

CASE-FINDING has been recognized for a long time as one of the chief means of tuberculosis control, and roentgen examination of the chest is the one dependable and accepted method for case-finding. Photofluorography is now perfected to such a degree that mass surveys of very large units of the population are entirely practical. By "mass survey" we mean examination of the entire population, above fifteen years of age, of an entire city, county or state. Only a few such surveys have yet been made, the largest being the one which was carried out in Washington, D.C. from January 12 to July 1, 1948. A complete analysis of the results of the Washington survey will not be available for several months and the statistics given in this paper must be considered tentative and subject to future revision. Nevertheless, valuable experience was gained in the course of the survey and some conclusions are already justified. It is the purpose of this paper to try to make them available to others for guidance in similar surveys which are now being organized.

A total of 503,398 individuals had 70 mm. films made during the survey but at the present time only 454,114 are susceptible of the tentative analysis here presented. Elimination of 13,623 unsatisfactory films leaves a net total of 440,491 70 mm. films which were interpreted with the results given in Table I.

TABLE I

	Number	Per Cent
Total 70 mm. films interpreted	440,491	100.0
Negative	423,577	96.2
Total abnormal findings	16,403	3.8
Definite tuberculosis	4,405 (1.0%)	
Suspected tuberculosis	6,166 (1.4%)	
Cardiac cases	2,537 (0.6%)	
Other pathology	3,806 (0.8%)	

The 16,403 cases with positive findings had 14 by 17 inch films made, of which 197 were unsatisfactory. The results of interpretation of the remaining 16,206 are tabulated in Table II.

A significant fact disclosed by the Washington survey is the relation of the total number of cases of tuberculosis disclosed by the survey to the cases registered at the local Health Department as tuberculosis. Of the more than 6,000 cases, only 567

* Presented at the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14–17, 1948.

were on the tuberculosis registry, leaving about 5,600 cases previously unknown to the Health Department of which number 83 to 85 per cent are in a minimal stage and about 10 per cent only moderately advanced.

The question has been raised recently as to the practical value of the mass survey method, which requires the examination of such a large number of non-tuberculous individuals to screen out a relatively small

TABLE II

	Number	Per Cent
Total 14″×17″ films	16,206	3.8
Negative	5,996	1.4
Tuberculosis	6,401	1.5
Total definite tuberculosis	5,352	1.3
Minimal	4,464 (83.4%)	
Moderately advanced	564 (9.8%)	
Far advanced	123 (2.3%)	
Other tuberculosis	241 (4.5%)	
Suspected tuberculosis	1,049	0.2
Cardiac cases	1,540	0.3
Other pathology	2,269	0.5

percentage of cases of tuberculosis. There seems to be little doubt of the value of a method which discloses over 5,000 people in a city the size of Washington who have tuberculosis, previously unknown, the great majority of them at an early stage of the disease. It is true that examination of selected groups of the population in which the incidence of tuberculosis is known to be high will yield much higher percentages of positive cases. The practice of examining the chest of all patients who are admitted to general hospitals is proving a fruitful case-finding method, and very recently reports have been made of the high incidence of tuberculosis among the patients who seek the advice of general practitioners. Any method that discloses cases of tuberculosis is valuable and should be used wherever practicable. There is little doubt, however, that the final control of tuberculosis will depend upon well organized, systematic mass surveys supplemented by persistent examination of selected groups in which the incidence is known to be high.

The aspects of the problem which needs the greatest emphasis at the present time is one which seems obvious but which in practice has not been dealt with in any systematic or adequate manner, that is, the follow-up, management and treatment of the individual patient once the disease is discovered. It must be increasingly appreciated that the finding of the case is only the beginning of a mass survey. The local Health Department must have a central place in tuberculosis control for the registry, hospitalization and laboratory service for the tuberculous patient, but the tendency to throw the entire responsibility for follow-up and management upon it must be combatted. One of the most important lessons learned in both the Minneapolis and Washington surveys is the fact that the success of a survey and the final control of tuberculosis is largely the responsibility of the medical profession. Such responsibility rests especially upon the general practitioner, the specialist in diseases of the lungs and the radiologist.

The physician's responsibility begins during the survey itself, not only to give invaluable assistance in the organized case-finding effort but to initiate the program for follow-up and management which must continue long after the actual survey is closed.

An essential part of the organization of a Mass Survey is the Medical-Technical Committee. Its chairman should be a member of the Executive Committee of the Survey and through him and appropriate subcommittee chairmen the Medical-Technical Committee can maintain an effective liaison with the Director of the Survey, the Operations Committee, the Publicity Committee, the local Health Department and the local Medical Society. For the Washington Survey the Medical-Technical Committee was organized into the following subcommittees:

I. Subcommittee of Medical Consultants.
II. Subcommittee on Medical Information.
III. Subcommittee on Diagnostic Standards.
IV. Subcommittee on Cooperation with the Medical Profession.
V. Subcommittee on Management of Positive and Suspicious Cases.
VI. Subcommittee on Nursing Service.
VII. Subcommittee on Social Service.

The *Subcommittee of Medical Consultants* consists of physicians qualified to advise the Director of the Survey on all matters of general medical policy; to give guidance and advice to the physicians who are interpreting the films and to those who are classifying the patients; and to provide consultants, either individual consultants or a medical board, in cases of unusual difficulty for which private consultants are not available. This subcommittee must continue to function for a long period, probably at least two years, after the Sur vey is finished to advise the Director of Tuberculosis of the Health Department concerning the management and classification of difficult cases. It should be stated here that in order to provide for continuity of policy and action it is advantageous that the Director of Tuberculosis of the local Health Department should be the Director of the Survey.

The *Subcommittee on Medical Information*, through its chairman, maintains close relations with the general Publicity Committee of the Survey and is the source of medical information for that committee and for other committee chairmen.

The *Subcommittee on Diagnostic Standards and Technique* is charged with the duties of establishing a system of standards and nomenclature for reports on the interpretation of films; to advise concerning the procedure to be followed in the roentgen examination of positive and suspicious cases; and to confer with and advise technicians on the technical problems which may arise.

The following standard nomenclature was adopted for the Washington Survey:

1. The findings on the 70 mm. film are reported as "negative" or "positive."
2. For report on impression of activity on the 14 by 17 inch film the following classification is used:
 a. Active { Minimal / Moderately advanced / Far advanced }
 b. Questionably active.
 c. Inactive.
 d. Questionably inactive.
 e. Activity to be determined.

It was agreed that the usual parenchymal and hilum primary tuberculosis complexes are not to be reported. Adoption of a uniform procedure for examination of positive and suspicious cases necessitates the use of form letters which must be carefully phrased in order to avoid ambiguity and to minimize misunderstanding on the part of patients and private physicians, and to prevent undue emotional disturbances on the part of patients. Formulation of such letters was one of the duties of the Subcommittee on Diagnostic Standards and Technique.

The *Subcommittee on Cooperation with the Medical Profession* is charged with duties which are essential to the success of a mass survey. Since a large percentage of tuberculous patients found in the survey are treated by private physicians, it is one of the most important duties of the Medical Technical Committee to secure cooperation of the general medical profession. The natural and most effective approach is through the local Medical Society. Approval and support of the Survey by the Tuberculosis Committee of the Medical Society should be followed by approval by the Executive Board and finally by the Society itself, and such approval should be made known to every member of the Society. The effort is facilitated if, as was the

case in Washington, the chairman of the Tuberculosis Committee of the Medical Society is also the chairman of the Subcommittee on Cooperation with the Medical Profession. It is also important to have the President of the Medical Society a member of the Executive Committee of the Survey. Information is disseminated to the members of the medical profession by means of editorials and news items in the local medical journal and bulletins and by letters mailed directly from time to time to every registered physician in the community, or enclosed with the regular or special notices sent out from the Medical Society office.

The *Subcommittee on Management of Positive and Suspicious Cases.* The main purpose of this committee is indicated by its name. Its functions are largely educational. It soon becomes apparent to anyone engaged in the work of tuberculosis control that there is great need for education of both the public and the general medical profession in modern methods of care of the tuberculous patient. Early in the Washington Survey this committee formulated in considerable detail recommendations for management and treatment of tuberculosis to the end that both clinic patients and those under the care of private physicians might have the benefit of the most recent knowledge and practice in the medical, nursing, and social service fields. A summary of these recommendations was sent to every registered physician and the complete recommendations were made available to any physician who requested a copy.

The following is an outline, necessarily brief, which indicates the scope of the committee's recommendations.

I. *Initial Report of Abnormal Findings to the Patient.* Following the 14 by 17 inch film each patient should be interviewed by a competent chest physician. His explanation should include:
 1. A brief explanation of the roentgen findings and what they *may mean.*
 2. Reassurance of the patient to allay *unreasonable* fears, without *minimizing* the serious nature of the lesion.
 3. An explanation of need for further clinical and laboratory study.
 4. A clear statement concerning the contagious nature of the disease, especially is sputum is positive.
 5. Explanation of need for reliance on advice of his physician.

II. *Clinical Study and Evaluation by the Private Physician or Public Health Clinic.*
 1. Clinical history.
 2. Physical examination.
 3. Additional chest roentgen studies. Fluoroscopy, laminagraphy, bronchography, etc.
 4. Tuberculin testing.
 5. Laboratory studies. Sputum, gastric lavage, etc.
 6. Special diagnostic studies. Bronchoscopy, biopsy.

III. *Nursing Investigation.*
 1. Contact investigation for source cases.
 2. To find evidence of spread to household or other associates.
 3. To identify health or economic conditions which may influence treatment or prognosis.
 4. To prescribe proper anticontagious regimens.
 5. To lay groundwork for subsequent observation and treatment, hospitalization, etc.
 6. To allay unreasonable fears.

IV. *Medical Social Work and Rehabilitation.*
 1. To provide for relief of economic distress.
 2. To assist in adjustment of family and household problems.
 3. Placement in suitable occupations.
 4. Provide for hospitalization when necessary.

V. *Treatment.*
 1. To provide standards for a clinical division between
 a. Hospitalization for treatment.
 b. Hospitalization for isolation.
 c. Home care and isolation.
 d. Clinical and roentgen observation.
 e. Discharge.
 f. Transfer for medical observation.

Under all of the above headings and sub-headings the committee's report gives detailed recommendations for proper procedures to be followed.*

The following observations and conclusions are based upon experience during and following the recent Washington, D. C. Chest Survey:

1. The ultimate effect of a chest survey campaign will depend largely upon the subsequent management and treatment of the cases disclosed by the Survey. This responsibility falls not only upon the local Health Department but particularly upon the physicians of the community.

2. Radiologists and chest physicians occupy key positions in the discovery, the differential diagnosis and the treatment of tuberculosis. Both should have an active part in the organization and conduct of case-finding campaigns and in subsequent plans for follow-up and management of the cases found. They have a special responsibility to assist in the dissemination of information to the general profession. Attention is directed especially to the following points:

a. Evaluation of a case with regard to activity and type of treatment to be instituted should not be based upon roentgen examination alone and never upon a single film.

b. Roentgen examination of the chest in frank or suspected tuberculous lesions is too often carried out in a casual or routine manner. Good stereoscopic films are important but the roentgenologist has not met his full responsibility in a case until he has exhausted every means that his method affords to throw every possible light on the extent and nature of the lesion. This includes comparison, whenever possible, with films previously made; routine examination in oblique and lateral projections and often in the lordotic posture; body section roentgenograms whenever there is the slightest question of the presence of cavity or tumor mass; and bronchography whenever indicated.

3. The differential diagnosis between tuberculous and non-tuberculous lesions must be approached with great care. Too many cases of atypical pneumonia are being diagnosed as tuberculosis and hurried into sanatorium treatment, and too often there is delay in operation on early bronchogenic carcinoma because atelectasis is mistaken for tuberculous consolidation. Such mistakes can usually be avoided by a proper appreciation of the value of the tuberculin test, the significance of the absence of tubercle bacilli in repeated examinations of the sputum and by more frequent bronchoscopic and biopsy examinations.

4. The Washington Survey has demonstrated a definite value of the mass survey in disclosing the presence of a considerable number of lesions within the chest other than tuberculosis. There were 1,540 cases (0.3 per cent of the total number examined) who showed definite abnormalities in the size and contour of the heart. All of these were referred to their physicians for further study. There were 2,269 cases, excluding the cardiac cases (0.5 per cent of the total number examined) who showed lesions other than tuberculosis. No definite statistics are available regarding these but some were diagnosed as bronchogenic carcinoma, some as lymphoblastoma, one as adenoma of a bronchus, two as solitary bronchogenic cysts, and several as bronchiectasis. The survey thus has a considerable value in disclosing diseases other than tuberculosis.

5. The Survey emphasized the great importance of education of the general practitioner in modern methods of diagnosis and treatment of tuberculosis. He must learn to appreciate the value and limitations of roentgen examination of the chest; the indications for special types of examination (tuberculin testing, laboratory

* The complete report will be published for general distribution in one of the Public Health Reports issued by the Tuberculosis Control Division of the United States Public Health Service.

tests, etc.); and the criteria upon which the type of treatment can be based. He must realize his responsibility to cooperate with the Health Department by making periodic reports and furnishing other data on cases under his care. He must inform himself of facilities available in his community in the nursing and social service fields for follow-up and care of his patients and make full use of such services.

6. Finally, the Survey served to bring home to general practitioner and specialist the fact that the physician as a citizen owes a duty to his community to take a leading part in efforts to establish adequate hospital and public health department facilities and personnel for the care of the tuberculous patients of the community.

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DISCUSSION

DR. W. EDWARD CHAMBERLAIN, Philadelphia, Pa. It augurs well for the future of our country when men of the caliber of Arthur Christie devote time and energy to the welfare of the public. Dr. Christie has put the emphasis where it belongs in this matter of mass roentgen surveys for tuberculosis case-finding, and the "follow-through" that is so important in this kind of work. It is reassuring to see that his findings agree with some observations that we have made in Philadelphia.

The roentgen appearance is, of course, the most important single factor in the follow-through of cases of tuberculosis, not only for case-finding, but in every other aspect of tuberculosis control. As Dr. Christie has said so well today, however, it must not be allowed to stand by itself. We get into all sorts of difficulties if we do not correlate with the roentgen findings all of the other evidence that can be used to throw light upon a case of suspected tuberculosis.

The most important single factor, as Dr. Christie has said, is the follow-through, the care of the case after it has been found by the survey. It is rather disconcerting to discover that after many years of intensive effort to obtain a proper setup for the follow-through or the follow-up of these cases, the work is still not being done very well.

In Philadelphia, we know where the emphasis should be placed, and we have tried very hard to get these cases properly taken care of, but we are still in difficulties because the medical profession doesn't yet understand what it is all about and the patients are still ignorant in many cases. Recently we had our eyes opened once more to the place where the emphasis has to be put, by a little experiment we carried out.

We decided to find out what had happened to 108 consecutive cases in which the roentgen evidence was rather frightening, cases that were deemed, on the 70 mm. film, to be really important. In this evaluation that took place about a year after the cases were discovered, we found such things as this: that only 25 of the 108 had ever been told that they must enter a hospital. We found that another 25 of the 108 cases had become completely uncooperative and would not even let the public health nurse or medical social worker or the doctor talk to them. A number of them had disappeared from view, never to be found again. I could go on and give you more details but here is the important thing. The follow-through had not been done skillfully and had not been done rapidly enough. You can't expect a human being to believe that what you are talking to him about is important if you allow a considerable delay to take place between the time the film is made and the time you first approach him. He is going to say, "If it is as important as you say, why did you let two or three months go by before you caught up with me?"

And there is yet another difficulty in this important work of tuberculosis control,—the fact that no two doctors seem to think alike on the question of what to do about a case of tuberculosis after the survey roentgen study has picked it out.

I want to say that this paper was timely and authoritative and it will help us to impress the public health authorities, in municipalities and in the nation, with the great importance of having a proper machinery for follow-up and follow-through *before* we begin to take roentgen survey films and find cases of tuberculosis.

THE VALUE OF ROENTGENOLOGY IN THE PROGNOSIS OF MINIMAL TUBERCULOSIS*

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RECENT reports have aroused much discussion as to the accuracy of estimation of activity in tuberculous lesions of minimal extent on the basis of interpretation of initial chest roentgenograms. In the current mass roentgen-ray survey programs such estimates are commonly made, although, as a rule, safeguarded with cautionary qualifications.

A well known and widely quoted paper by Birkelo, Chamberlain, *et al.*[1] on "Tuberculosis Case Finding" clearly indicates the fallibility of original estimates, pointing out that qualified roentgenologists differed greatly in their interpretation of individual roentgenograms, and that a roentgenologist often fails to confirm his own original diagnosis when he reads a roentgenogram unknowingly for the second time.

Recently Birkelo and Rague[2] have reviewed the subject on the basis of a study of 699 cases of minimal tuberculosis followed for two to five years, and they come to the conclusion that a relatively high degree of accuracy in determination of activity from the first roentgenogram is possible. Reproductions of roentgenograms from selected cases, which were in many instances microfilms, illustrate both their successes and failures in original estimate.

The following paper, representing the first of a projected series, deals with the same subject on a statistical basis. It presents a study of an even larger number of cases over a longer period of time.

The object in this series of papers is to examine the prognostic value of the various characteristics, roentgenological, symptomatological, socio-economic, and personal, which are involved in the interpretation of a minimal lesion. This paper is concerned solely with the prognostic value of the roentgenologist's diagnoses: "active," "of questionable clinical significance," and "inactive, of no clinical significance." An effort is made to determine whether the fate of persons placed in these three groups on the basis of roentgen diagnosis differed in any statistically significant way and, if so, to discover whether this difference was medically significant or compatible with a large error.

METHOD AND SCOPE OF STUDY

The data used in this study consisted of roentgenograms of all minimal cases diagnosed in the chest clinic of the Henry Phipps Institute from 1926 to 1945, inclusive, with the following exceptions:

1. Fourteen patients who had had previous treatment before coming to the Phipps Institute.
2. Thirteen patients whose original film readings at the Institute had been lost, or whose charts contained inadequate information.
3. Two Chinese patients who were omitted in order to limit the study to the two principal categories of white and Negro.

The number of patients studied totalled exactly 1,100; according to Table 1, these patients were rather evenly distributed among white and Negro males and females. The follow-up period for these patients ranged from one month to nineteen years.

These cases were judged to be of minimal extent on the basis of a classification of stage of disease made in 1938 of all Phipps Institute patients examined up to that date. Since then all roentgenograms have

* This study was aided by a grant from the Office of Naval Research.
† During the course of this investigation Doctor Campbell died. He was responsible for much of the organization of the study and collaborated in its prosecution with unfailing spirit as long as his strength permitted.

been classified and coded when read. The work involved in twenty years of coding was both difficult and laborious. Without it, however, this study would have been impossible.

From the 1,100 case histories, certain data relevant to the present paper were extracted.

1. *The classification in regard to clinical status* made by the roentgenologist at the time the first diagnosis of minimal tuberculosis was made. In general, only the first roentgenogram was considered; but if additional special roentgenograms were requested (apical or stereoscopic) or if the first was technically unsatisfactory, these were included with the first roentgenogram. Since 1938 all diagnoses have been classified at the time they were made, minimal lesions being coded as active, of questionable significance, and as inactive. Minimal cases diagnosed during this period presented no difficulty in classification and no possibility of personal error on the part of the authors. The other cases which were diagnosed before 1938 were classified in the same three groups on the following basis:

a. The only cases coded as active were those in which the roentgenologist in his written report had used one of these phrases, "This lesion is active," "This appears to be dangerous," "This requires treatment," or when the adjectives "soft" or "flocculent" had been used to describe the infiltration. In addition, those who had had a roentgenogram negative for tuberculosis less than one year before were included as active unless the roentgenologist definitely stated that the lesion seen was not active.
b. Only those cases were classified as inactive in which the phrase "of no clinical significance" was used in the comment, or the words "old," "fibrotic," or "hard" were used to describe the infiltration.
c. All other cases were classified as of questionable clinical significance.

TABLE I

CASES OF MINIMAL TUBERCULOSIS OF SPECIFIED ACTIVITY WHICH WERE INCLUDED IN THIS STUDY, CLASSIFIED BY SEX AND COLOR: HENRY PHIPPS INSTITUTE, 1926–1945

Sex and Color	Cases of Minimal Tuberculosis of Specified Activity			
	Total	Active	Of questionable significance	Inactive
Both rates	1,100	267	509	324
White	625	123	286	216
Male	320	50	152	118
Female	305	73	134	98
Negro	475	144	223	108
Male	274	80	134	60
Female	201	64	89	48

With such a technique the possibility admittedly exists that personal bias, as regards the value of roentgenology, might have influenced the classification. It is believed, however, that certain factors minimized this possibility. For example, one author who did the majority of the selections was a stranger to the clinic and the subsequent fate of a patient was unknown

to him upon his first reading of the roentgen report. Moreover, all doubtful cases were discussed by two or more of the authors and all 1,100 cases were carefully reviewed with this possibility in mind.

2. *The following dates and data expressing the number of months after the first diagnosis of tuberculosis:*

a. The date of the first roentgenogram showing progression to a moderately advanced stage (x)
b. The date of the last roentgenogram showing a minimal lesion (y)
c. The date of death, if due to tuberculosis (q)
d. The date on which the patient was last known to be alive (r)

From these dates the date of "corrected progression" was calculated from the formula:

$$y+\frac{x-y}{2}.$$

In the few cases where the patient died from tuberculosis before any roentgenogram showing a moderately advanced lesion had been taken, the date of "corrected progression" was calculated by simple proportion, using data from those of the same sex-color roentgenological group who had died. A factor was first calculated for each group from the formula $(x-y)/(q-y)$ and from this, "x" in any other case could be deduced when "q" and "y" were known. This factor is thought to be sufficiently accurate for the purposes of this paper. Only 13 such cases were included in the study.

From these figures two "rates" were calculated per 100 person-years of observation:

1. The number progressing to the moderately advanced stage (P rate).
2. The number dying from tuberculosis (D rate).

For the two rates different "observation" times were used, since it is clearly impossible to say without roentgenological evidence that a lesion has not progressed to the moderately advanced stage, though there may be good reason for believing that the patient is still alive. For this reason "x" and "y" were used in "P" rates and "q" and "r" in "D" rates.

In addition, "D" rates were calculated in another way on the assumption that the data covering deaths were nearly complete because of the excellent cooperation between the local division of tuberculosis and the chest clinic. Notification is sent to the Phipps Institute of all death certificates filed for persons dying of tuberculosis in the area, if there has been any record of previous association with the Institute. In addition, details of other such deaths occurring outside Philadelphia are often discovered during routine visits. For these reasons a death rate per 100 observation person-years for five years has been calculated, assuming that no other deaths from tuberculosis occurred. These two rates can be considered as maximal and minimal values; therefore, an average of these two rates has been used throughout the study. A similar line of argument does not hold for progressions.

It is recognized that some personal error exists in reading roentgenograms as showing a change to moderately advanced disease; moreover, a roentgenologist might unconsciously tend to improve his score by "overreading" those roentgenograms he had originally diagnosed active, when they approached the moderately advanced category. It is, however, necessary to have some intermediate reading since the number of deaths is statistically rather small.

The only practical alternative is to use Reisner and Downes'[3] "definite progressions," and this alternative is believed to be even more liable to error. This belief has been fostered by a recent demonstration of roentgenograms at the Central Cooperative Clinic, Temple University School of Medicine. This demonstration showed apparent "definite progression" within the minimal limits in roentgenograms taken of the same individual at a few minutes' interval as a result of a slight variation in technique.

While the material in this study is con-

fidently believed to be unselective, by including all minimal cases, whatever their follow up, the authors have been forced to face other difficulties. The problem is only partially solved by using rates per 100 person-years, since the probability of progressing differs considerably in the various years following diagnosis;* thus, every person-year of observation has not the same value in terms of "risk." The situation could have been improved statistically by including, for example, only those cases on which we had a five year follow up, but this policy would have led to a most undesirable degree of selection. It is believed that the error has been minimized by calculating the rates per 100 person-years for each year, but it is not a completely satisfactory solution.

Before considering the results, two further points must be made:

1. These roentgenograms were not read under experimental conditions; they were read in the normal course of the clinic's work and the patient's chart was usually available. This chart gives information as to age, sex, color, marital status, exposure to tuberculosis, medical history, and clinical examination. The results of sputum examination and tuberculin testing were not available at the time the roentgenograms were read. It is impossible at this time to determine whether the roentgenologist was helped or hindered by having this information. The extent to which it might have helped will be discussed in a later paper. This study is concerned with the practical value of roentgenology under clinic conditions.

2. This type of analysis is a severe test for a roentgenologist. In the first place he has only one roentgenogram from which to make up his mind. In the second he gets no credit for those cases of questionable significance which he diagnoses as becoming active after a period of observation during which treatment is refused and the disease progresses. In the third place a roentgenologist, statistically, conspires to hide the evidence of his success. Patients with active disease are advised to rest and successful treatment means that there is no progression. It is also true that successful treatment may conceal an error in cases in which the gravity was actually overestimated. In South Philadelphia, however, for psychological and socio-economic reasons, large numbers of patients with active

* See Figures 1 and 2.

TABLE II

RATIO OF PROGRESSIONS TO PERSON-OBSERVATION YEARS* AND PROGRESSION RATES PER 100 PERSON-OBSERVATION-YEARS AMONG CASES OF MINIMAL TUBERCULOSIS OF SPECIFIED ACTIVITY, CLASSIFIED BY SEX AND COLOR

Sex and Color	Ratio of Progressions to Person-Observation Years*			Progression Rates per 100 Observation Years*		
	Cases of active minimal tuberculosis	Cases of minimal tuberculosis of questionable significance	Cases of minimal inactive tuberculosis	Cases of active minimal tuberculosis	Cases of minimal tuberculosis of questionable significance	Cases of minimal inactive tuberculosis
White						
Male	21:111.8	6:365.3	5:278.5	18.8	1.6	1.8
Female	25:197.0	14:356.0	1:264.6	12.7	3.9	0.4
Negro						
Male	35:143.8	16:182.7	0:120.8	24.3	8.8	0
Female	30:138.3	9:227.5	2:101.8	21.7	4.0	2.0

* Limited in each case to five years.

minimal tuberculosis refuse treatment, and really adequate treatment is rare; therefore, it is probable that roentgenologists, in this one respect, fare better in estimating prognosis in South Philadelphia than elsewhere.

ANALYSIS OF FINDINGS

The Value of Roentgenology

Data for the four sex-color groups have been calculated separately to eliminate these variables. Table I shows the distribution among the various groups. Table II shows the number of progressions per 100 person-observation years in these groups. A limit of five years was placed on any individual observation period. Table III shows the death rates in a similar way. As previously explained, these are averages between the maximum and minimum values.

Figures 1 and 2 show the number of progressions per 100 person-observation years for each individual year, for the first five years after diagnosis, in the various groups. To save space, the numerical data for these figures have not been published, but they are available at the Henry Phipps Institute.

Both the orderly numerical descent in the tables and the striking differences in the curves suggest that these roentgenological estimates of activity have been of value at the Phipps Institute, but, before drawing definite conclusions, certain points must be investigated.

TABLE III

AVERAGED* DEATH RATES PER 100 PERSON-EXPERIENCE-YEARS AMONG CASES OF MINIMAL TUBERCULOSIS OF SPECIFIED ACTIVITY, CLASSIFIED BY SEX AND COLOR

Sex and Color	Cases of Active Minimal Tuberculosis			Cases of Minimal Tuberculosis of Questionable Significance			Cases of Inactive Minimal Tuberculosis		
	Number of deaths	Averaged* death rates	Average of—	Number of deaths	Averaged* death rates	Average of—	Number of deaths	Averaged* death rates	Average of—
White Male	3	1.3	{1.6 1.0	2	0.4	{0.5 0.3	—	0.1	{— 0.2
Female	4	1.5	{1.3 1.6	4	0.6	{0.8 0.4	—	—	{— —
Negro Male	25	5.4	{10.7 0.0	3	1.3	{1.1 1.4	—	1.5	{— 2.9
Female	14	4.1	{6.2 2.0	4	0.7	{1.4 0.0	1	0.4	{0.7 —

* See page 155 of text for explanation.

1. The correlation between "*D*" rates and "*P*" rates. As death is a much more definite measure than progression, it is important to know how closely the two measurements agree. This problem was studied by the following method: Expected deaths were calculated by applying the rates of progression to the exposure times for deaths and then reducing the results to the same numerical total as the deaths. The expected deaths were then compared with the actual deaths by chi squared.

Fisher's tables indicate that the probability of obtaining poorer agreement by chance is 75 per cent for whites (both

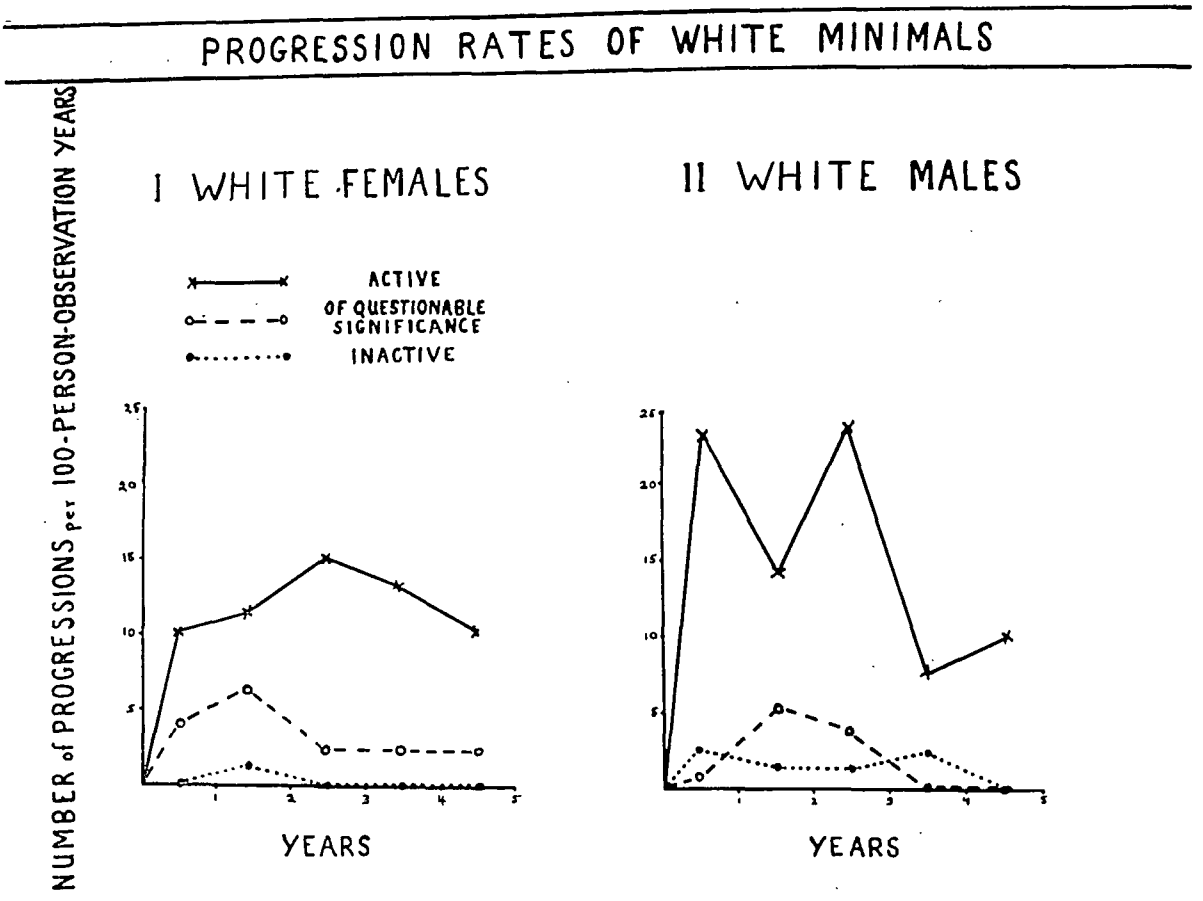

PROGRESSION RATES OF WHITE MINIMALS
NUMBER of PROGRESSIONS per 100-PERSON-OBSERVATION YEARS
I WHITE FEMALES
II WHITE MALES
ACTIVE
OF QUESTIONABLE SIGNIFICANCE
INACTIVE
YEARS
YEARS

FIG. 1

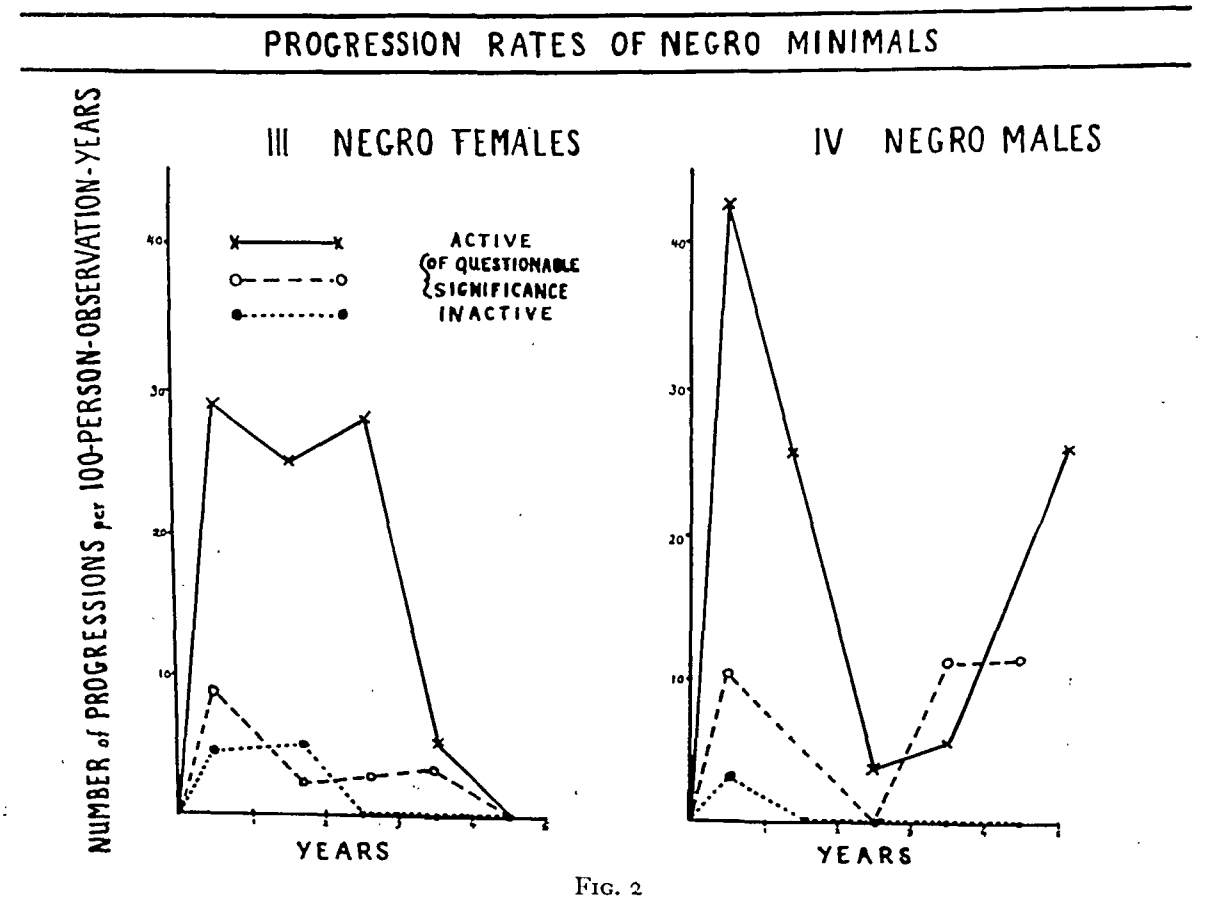

PROGRESSION RATES OF NEGRO MINIMALS
NUMBER of PROGRESSIONS per 100-PERSON-OBSERVATION-YEARS
III NEGRO FEMALES
IV NEGRO MALES
ACTIVE
OF QUESTIONABLE SIGNIFICANCE
INACTIVE
YEARS
YEARS

FIG. 2

sexes combined to give 5 degrees of freedom) and 15 per cent for Negroes. These results are perfectly consistent with the hypothesis that progression rates are a good measure of death rates and serve to strengthen the conclusions drawn from a detailed study of progression rates.

2. *Influence of case history on roentgenologist's diagnosis.* Among the four active groups a considerable number of cases were found which, when diagnosed, had had roentgenograms negative for tuberculosis less than one year before. In these cases it was thought that the history of the lesion as well as its flocculence might have influenced the roentgenologist. One does not suggest that skill is not required to distinguish these early lesions; it is a different type of skill, however, and as such should be investigated.

Table IV shows the summarized results of the "*P*" rates after subtraction of these cases with previous negative roentgenograms, and summarizes the corresponding "*D*" rates.

It is clear that the subtraction has made little general difference; the orderly numerical descent continues except in the case of the female white "*D*" rate where the number of deaths is very small. There seems no reason to believe that these cases have accounted for the roentgenologist's success.

3. *Extent to which the authors might unconsciously have helped the roentgenologist's score.* In spite of every precaution it is always possible that this bias might have happened. To investigate this possibility, the data were divided into the two decades 1926–1935 and 1936–1945. In the first decade all the cases were classified by the authors on the basis already described. In the second, the majority were coded at the time they were read by the roentgenologist while the remainder were diagnosed by the roentgenologist, using the same terminology as was later embodied in the code. The results are shown in Table v.

The most important feature is the regular numerical descent in the 1936–1945 decade, in which the division of the cases into the three groups was uninfluenced by the authors. Too much attention should not be paid to the differences and resemblances between the two decades. Many other factors varied in these two periods. One saw the depression; the other the full employment of war time. Roentgenological technique has improved and with it probably the accuracy in diagnosis of minimal

TABLE IV

EFFECT ON PROGRESSION RATES* AND DEATH RATES* OF EXCLUDING ACTIVE MINIMAL CASES WITH FILMS NEGATIVE FOR TUBERCULOSIS LESS THAN ONE YEAR BEFORE DIAGNOSIS, CLASSIFIED BY SEX AND COLOR

Sex and Color Active†	Progression Rates* Among Cases of Active Minimal Tuberculosis		Death Rates* Among Cases of Active Minimal Tuberculosis	
	Before exclusion	After exclusion	Before exclusion	After exclusion
White				
Male	18.8	18.1	1.6	1.6
Female	12.7	11.4	1.3	0.7
Negro				
Male	24.3	24.6	10.7	10.4
Female	21.7	19.7	6.2	5.4

* Per 100 observation years.
† Tables for "Of questionable significance" and for "Inactive" available at the Henry Phipps Institute.

lesions. It is probable, too, that theoretical ideas with reference to the treatment of minimal cases, if not always the practical results, have improved considerably during these two decades.

The question now arises as to what extent these various differences can be tested statistically for significance. The number of progressions and deaths per 100 person-years in five years has finally been chosen as the best figure for statistical treatments, though a case could be argued for a shorter period, particularly for the Negroes. The results are shown in Tables VI-A and VI-B.

Considering the small size of the groups, the number showing a ratio of difference to standard error of more than 2 is very striking. The lesser degree of significance among the death rates is to be expected because of the smaller number of deaths. The greater significance found among Negroes is presumably due to the fact that in this group treatment has interfered less with the natural history of disease.

The roentgenological interpretation of films of minimal lesions as carried out at the Phipps Institute has thus been of value in estimating prognosis. It appears to have been of greater value in differentiating between active cases and those of questionable significance than between the latter and inactive cases.

The Roentgenologist's Error

In determining such errors no rules are available for guidance, a fact which is in itself a silent witness to the medical profession's faith in the roentgen examination. Therefore, the following yardstick has been devised which, if anything, errs on the side of severity. The following are arbitrarily considered errors:

1. "Inactive" cases which progressed in five years.
2. Cases "of questionable clinical significance" which progressed in two years.
3. "Active" cases which in the absence of any treatment did not progress.

 The above three groups constituted the *"minimal error" in diagnosis.*
4. One must, however, consider the possible error concealed in those active cases which had treatment and which did not progress. No one knows what would have happened if they had had *no* treatment; therefore, such cases as the above must be included in order to calculate the "maximal error."

The results are shown in Tables VII and VIII which reveal, as was expected, a considerable error. This method of approach

TABLE V

PROGRESSION RATES AND DEATH RATES PER 100 PERSON-OBSERVATION-YEARS AMONG CASES OF MINIMAL TUBERCULOSIS OF SPECIFIED ACTIVITY, CLASSIFIED BY RACE AND DECADE STUDIED

Race and Decade Studied	Cases of Active Minimal Tuberculosis		Cases of Minimal Tuberculosis of Questionable Significance		Cases of Inactive Minimal Tuberculosis	
	Progression rates	Death rates	Progression rates	Death rates	Progression rates	Death rates
White						
1926–1935	15.8	1.3	2.5	0.7	0.7	—
1936–1945	13.3	1.7	3.3	0.3	3.0	—
Negro						
1926–1935	20.2	8.1	3.2	2.0	1.0	0.9
1936–1945	24.4	8.7	7.4	1.0	0.8	—

TABLE VI-A

SIGNIFICANCE OF DIFFERENCES BETWEEN THE PROGRESSION RATES PER 100 PERSON-OBSERVATION-YEARS AMONG CASES OF ACTIVE MINIMAL TUBERCULOSIS AND MINIMAL CASES OF QUESTIONABLE SIGNIFICANCE CLASSIFIED BY SEX AND COLOR

Sex and Color	Cases of Active Minimal Tuberculosis		Cases of Minimal Tuberculosis of Questionable Significance		Standard Error of Difference	Ratio of Difference to Standard Error
	Ratio of progressions to observation years	Progression rate	Ratio of progressions to observation years	Progression rate		
White						
Male	21:111.8	18.8	6:365.3	1.6	4.15	4.1
Female	25:197.0	12.7	14:360.9	3.7	2.74	3.3
Negro						
Male	35:143.8	24.3	16:182.7	8.8	4.66	3.3
Female	30:140.4	21.6	9:227.5	4.0	4.15	4.2

TABLE VI-B

SIGNIFICANCE OF DIFFERENCES BETWEEN THE PROGRESSION RATES PER 100 PERSON-OBSERVATION-YEARS AMONG MINIMAL CASES OF QUESTIONABLE SIGNIFICANCE AND INACTIVE CASES OF MINIMAL TUBERCULOSIS, CLASSIFIED BY SEX AND COLOR

Sex and Color	Cases of Minimal Tuberculosis of Questionable Significance		Cases of Inactive Minimal Tuberculosis		Standard Error of Difference	Ratio of Difference to Standard Error
	Ratio of progressions to observation years	Progression rate	Ratio of progressions to observation years	Progression rate		
White						
Male	6:365.3	1.6	5:278.5	1.8	1.05	−0.2*
Female	14:360.9	3.7	1:264.6	0.4	1.10	2.6
Negro						
Male	16:182.7	8.8	0:120.8	—	2.19	4.0
Female	9:227.5	4.0	2:101.8	2.0	1.92	1.0

* This is the only case in which the difference in rates contradicts the roentgenologist, and this difference is completely insignificant (significance at 5 per cent level is given by ratio of 1.96).

is, however, not wholly satisfactory, since no allowance is made for the degree of accuracy which would have been achieved by pure chance; e.g., if a roentgenologist blindly shuffled the roentgenograms of minimal cases into three boxes, he would inevitably toss some into the right one. Table IX shows the female white patients, classified by a roentgenologist's diagnosis and progression.

The "errors" appear with an asterisk in the upper right and lower left corners. These errors are not to be compared with those expected if roentgen diagnosis had no meaning—if roentgenological classification had no relation to later progression—in short, with the results expected from the "blind" roentgenologist.

To be fair to the Phipps roentgenologist, however, the "blind" roentgenologist should be forced to have 67 cases diagnosed as active, 119 questionable cases, and 73

diagnosed as inactive. Since the "blind" roentgenologist would assign diagnoses at random, each case would have 67 chances in 259 of being called active. Thus, of the 24 cases which progressed in two years, on the average one would expect 6.2 (67/259×24) to be called active. Table x shows the results obtained by proceeding in this way. The results of the diagnoses made by the Phipps roentgenologist and by the "blind" roentgenologist, as shown in Table xi, can now be compared.

The score is merely the percentage of the "blind" roentgenologist's errors which the Phipps roentgenologist avoided making. The perfect score is 100 and a score of 0 is no better than chance. A really bad diagnostic method would have resulted in negative scores.

For the other groups the Phipps roentgenologist did somewhat better on the average, as is shown in Table xii. The scores for each type of error differ substantially from group to group, but the

Table VII

ERRORS IN DIAGNOSIS OF SPECIFIED TYPE* AND NUMBER AT RISK,† CLASSIFIED BY SEX AND COLOR

Sex and Color	Inactive Minimal Cases		Minimal Cases of Questionable Significance		Active Minimal Cases		Active Minimal Cases Which Had Treatment and Which Did Not Progress
	Which progressed in five years	Number at risk†	Which progressed in two years	Number at risk†	Which did not progress**	Number at risk†‡	
White							
Male	5	78	4	122	5	43	17
Female	1	73	10	119	18	67	24
Negro							
Male	0	39	13	96	19	65	11
Female	2	29	7	73	12	54	12

* See description of errors 3 and 4 on page 160.
† Number at risk includes only those with a roentgenological follow up.
** In the absence of any treatment.
‡ Number at risk excludes those with inadequate data as to rest.

Table VIII

MAXIMAL AND MINIMAL ERRORS* IN DIAGNOSIS AND PERCENTAGE OF CASES AT RISK† WHICH WERE DIAGNOSED ERRONEOUSLY, CLASSIFIED BY SEX AND COLOR

Sex and Color	Cases of Minimal Tuberculosis at Risk†	Maximal Errors*		Minimal Errors*	
		Number	Per cent of cases at risk†	Number	Per cent of cases at risk†
White					
Male	243	31	12.0	14	5.8
Female	259	53	20.0	29	11.2
Negro					
Male	200	43	21.0	32	16.0
Female	156	33	21.0	21	13.5

* See description of errors 3 and 4 on page 160.
† Number at risk includes only those with a roentgenological follow up; those with inadequate data as to rest were excluded.

TABLE IX

CASES OF MINIMAL TUBERCULOSIS OF SPECIFIED ACTIVITY AMONG WHITE FEMALES,* CLASSIFIED BY PERIOD IN WHICH PROGRESSION OCCURRED

Period in Which Progression Occurred	Cases of Minimal Tuberculosis among White Females			
	Total†	Active	Of questionable significance	Inactive
Total	259	67	119	73
First two years after diagnosis	24	13	10**	1**
Next three years	16	12	4	0
Not in five years	219	42**	105	72

* Tables available for other groups at the Henry Phipps Institute.
† Total does not agree with Table 1 since inadequate follow-up cases (2 years) had to be excluded.
** Indicates a group of errors.

TABLE X

CASES OF MINIMAL TUBERCULOSIS OF SPECIFIED ACTIVITY AMONG WHITE FEMALES* WHICH WOULD HAVE BEEN DIAGNOSED BY A "BLIND" ROENTGENOLOGIST, CLASSIFIED BY PERIOD IN WHICH PROGRESSION OCCURRED

Period in Which Progression Occurred	Cases of Minimal Tuberculosis among White Females Which Would Have Been Diagnosed by a "Blind" Roentgenologist			
	Total	Active	Of questionable significance	Inactive
Total	259.0	67.0	119.0	73.0
First two years after diagnosis	24.0	6.2	11.0	6.8
Next three years	16.0	4.1	7.4	4.5
Not in five years	219.0	56.7	100.6	61.7

* Tables available for other groups at the Henry Phipps Institute.

TABLE XI

ERRORS MADE BY PHIPPS INSTITUTE AND "BLIND" ROENTGENOLOGIST* IN DIAGNOSING MINIMAL CASES OF TUBERCULOSIS AMONG WHITE FEMALES AND "SCORE" OF PHIPPS INSTITUTE ROENTGENOLOGIST, CLASSIFIED BY TYPE OF ERROR

Type of Error	Errors Made by Roentgenologist		"Score" (in Percentage) Made by Phipps Roentgenologist
	Phipps	"Blind"	
All types	53	79.0	42
Inactive cases which progressed in five years	1	11.3	91
Cases of questionable significance which progressed in two years	10	11.0	9
Active cases which did not progress†	42	56.7	26

* Tables available for other groups at the Henry Phipps Institute.
† See description of errors 3 and 4 on page 160.

TABLE XII

ERRORS MADE BY PHIPPS INSTITUTE AND "BLIND" ROENTGENOLOGIST IN DIAGNOSING MINIMAL CASES OF TUBERCULOSIS AMONG ALL SEX AND COLOR GROUPS AND "SCORE" MADE BY PHIPPS ROENTGENOLOGIST IN DIAGNOSING CASES IN SPECIFIED GROUP, CLASSIFIED BY TYPE OF ERROR

Type of Error	Errors Made by Roentgenologist		"Scores" (by Percentage) made by Phipps Roentgenologist in Diagnosing Cases in Specified Group				
	Phipps	"Blind"	All sex and race groups	Male white	Female white	Male Negro	Female Negro
All types	162	300.0	54	51	42	57	55
Inactive cases which progressed in five years	8	39.1	80	52	91	100	74
Cases of questionable significance which progressed in two years	34	56.5	40	60	9	38	52
Active cases which did not progress*	120	204.4	41	41	26	34	40

* See description of errors 3 and 4 on page 160.

samples are so small that the differences are not statistically significant.

In diagnosing inactive cases the Phipps roentgenologist's score was four-fifths of the way from blind chance to perfection, but in determining questionable and active cases his score was only two-fifths perfect. This result represents a good performance since the clinical desirability of an active diagnosis for a patient with probability one-half of progressing makes it inevitable that a competent roentgenologist will seem to overdiagnose active cases according to the definition of error. The earlier tables and discussion have shown how useful such performance can be clinically, even if it is far from perfection.

The figures from the paper of Birkelo and his colleagues[1] can be reanalyzed on a similar "blind" basis. The roentgenologists when "scored" as above for re-reading roentgenograms get a value of 70, which, as their task was easier, is in every way compatible with the results of this study. Although the details of this method are omitted from this report, they may be obtained either from Professor John Tukey at Princeton University or from the Henry Phipps Institute.

By both techniques it is clear that a considerable error exists in the roentgenologist's estimate of prognosis, but this finding in no way detracts from its value, as previously demonstrated.

SUMMARY

Eleven hundred cases of minimal tuberculosis, representing, with a few minor exceptions, all the cases of minimal tuberculosis diagnosed at the Henry Phipps Institute for the twenty years, 1926–1945, have been classified and followed up.

This paper has analyzed the results from the point of view of the prognostic value of the roentgenologist's opinion of activity at the time of the first roentgenogram. Both progression rates and death rates indicate that such opinions are of great value in determining the type of treatment for such cases.

The error of the roentgenologist has also been estimated by two different methods on the same roentgenograms. Both confirm the recently published opinion

that there is a considerable roentgenological error. The technique of comparison with the errors of a roentgenologist sorting roentgenograms blindly shows that the results are much better than those which would have been expected by chance; in particular, the error in the diagnosis of inactive minimal tuberculosis has been found to be small.

ACKNOWLEDGMENTS

This study is an end product of twenty years of cooperative work by all members of the staff of the chest clinic of the Henry Phipps Institute; among these staff members Dr. H. W. Hetherington should be mentioned particularly since he reported the majority of the roentgenograms on which this study is based.

The authors are also deeply indebted to Professor John Tukey, Consulting Statistician to the Office of Naval Research, and his colleagues of Princeton University for assistance in statistical analysis, to Miss E. Placentra for her assistance with the records, and to Dr. E. R. Long for critical review of the analysis at several stages in its development.

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VERTEBRAL ANGIOGRAPHY*

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WHILE attempting to perform angiograms by the percutaneous method (Shimidzu[27], Green and Arana[8]) occasionally the vertebral artery has been punctured instead of the carotid. The information obtained from these accidental vertebral angiograms is sometimes very useful. Thus, at our institution a previously unsuspected metastatic carcinoma of the thalamus has been disclosed (Fig. 2a). In another patient, with a traumatic cavernous-carotid fistula, the extent of collateral circulation was demonstrated (Fig. 3b) rendering less difficult the decision to ligate a carotid artery.

Recently we subjected a patient (Case IV), in whom a ruptured aneurysm was suspected, to bilateral percutaneous carotid arteriography without demonstrating a lesion. The desire to study the vessels of the posterior fossa in that case led to the development of a successful technique of deliberate percutaneous vertebral angiography.

ANATOMY

The vertebral artery is the first branch of the subclavian artery. It ascends vertically to the foramen transversarium of the sixth cervical vertebra, through which it passes, to run in the corresponding foramina of the higher cervical vertebrae, anterior to the emerging cervical nerves. After passing through the foramen in the transverse process of the atlas, it turns behind the articular process and lies in the groove on the posterior arch of the atlas. The artery pierces the atlanto-occipital membrane and dura mater to enter the skull through the foramen magnum. It lies first lateral to, then anterior to, the medulla oblongata and joins its fellow from the opposite side at the lower border of the pons to form the basilar artery. This passes ventral to the midline groove of the pons to divide into its terminal branches at the upper end of the pons. The major intracranial branches of the vertebral artery are:

1. Anterior spinal artery—joining with the one of the opposite side to run in front of the anterior median sulcus of the spinal cord.

2. Posterior spinal artery—coursing down the dorsal surface of the spinal cord medial to the emerging dorsal roots.

3. Posterior inferior cerebellar artery—supplying the undersurface of the cerebellum, the medulla oblongata, and part of the pons.

The major intracranial branches of the basilar artery are:

1. Anterior inferior cerebellar artery—supplying the undersurface of the cerebellum.

2. Internal auditory artery—passing into the internal auditory meatus.

3. Pontine branches.

4. Superior cerebellar artery—passing around the cerebral peduncle to the upper surface of the cerebellum.

5. Posterior cerebral artery—passing parallel to the superior cerebellar artery (separated from it by the oculomotor nerve and the tentorium cerebelli) to supply the basal ganglia, occipital lobe, and the inferior gyri of the temporal lobe.

In its first or non-osseous cervical portion, the vertebral artery lies immediately behind the vertebral and jugular veins (and the thoracic duct on the left). It lies between the longus colli and the scalenus anticus muscles. As it passes through the transverse processes it is accompanied by a venous plexus of vertebral veins and by sympathetic nerve fibers. After it leaves the foramen of the transverse process of the atlas, it lies in the suboccipital triangle

* From the Department of Neurology and Neurological Surgery, University of Illinois College of Medicine at the Illinois Neuropsychiatric Institute, Chicago, Illinois.

before passing through the dura mater.

The posterior portions of the transverse processes of the cervical vertebrae are shaped so that they form a virtually unbroken column of bone and articular surfaces, which for practical purposes, is impenetrable. Anteriorly, however, there are gaps between the surfaces of the adjacent transverse processes amounting to as much as one centimeter, crossed by the intertransverse muscles which cover the vertebral artery and vein as these pass from foramen to foramen. Through these spaces the vertebral artery may be entered by a needle inserted from in front.

TECHNIQUE

The entire procedure of vertebral angiography is carried out in the X-ray Department. After suitable premedication the patient is anesthetized with sodium pentothal by intravenous drip (0.2–0.5 per cent solution) (Teplinsky, Harris, Cassels and Sugar[30]). This is done in the supine position, on a cart which can be raised or lowered at will. An intratracheal tube is inserted. Then, in order to extend the neck, two pillows are placed under the upper thorax and the head is supported on a radiolucent cup or on a board which projects horizontally from the end of the cart. The cart is then placed so that the side of the patient's head rests against the vertically placed plate holder of the special head unit. Alternatively, films may be taken with any horizontally beamed roentgen-apparatus containing a Bucky grid or with a cassette and a Lysholm grid.

The shaved skin of the neck is cleansed with alcohol sponges. The operator's left thumb is placed lateral to the upper margin of the thyroid cartilage, pressing firmly downward, effectively separating the carotid sheath and its contents from the trachea until the transverse process of the fifth cervical vertebra is palpated. It is then easy to insert the needle through the skin and underlying fasciae until it rests on bone. The thumb can then be withdrawn, allowing the tissues to spring back into place. It is usually easy to palpate the lateral extremity of the transverse process and the needle point is directed laterally to reach this tip for orientation; this is also done even if the transverse process cannot be palpated from the outside. The needle point is then shifted medially about a centimeter to bring it approximately over the region of the foramen transversarium. Now, as the needle is cautiously advanced the point slips over the anterior superior margin of the process yet under the anterior inferior margin of the process above. It then passes into the foramen itself, where it usually engages the vertebral artery. Occasionally, the artery is encountered as it passes from foramen to foramen. At times the needle will pass completely through the artery; it should always be withdrawn slowly, therefore, in order that this be recognized.

A sharp medium bevel 17-gauge 3 inch (8 cm.) straight needle is attached by means of a Luer-Lok observation tube to a 6 inch (15 cm.) rubber stethoscope-tubing, the other end of which is tied to a two-way stopcock. This is connected to a 20 cc. syringe containing a 2.5 per cent solution of sodium citrate in water. The tubing and needle are filled with the solution prior to insertion through the skin to minimize the dangers of clot formation in the needle and air embolism. When the vertebral artery is entered there is a rush of bright red blood into the observation tube. If permitted, this blood will push its way into the syringe with sufficient force to expel the plunger. When venous channels are encountered, no such rush or pressure occurs. If, for some reason, the injection is not made immediately after blood is encountered, it may be necessary to remove the needle and irrigate it before reinsertion.

When the artery has been encountered and the needle tip properly secured by the fingers of the operator, the assistant replaces the citrated solution with a syringe containing 20 cc. of a 35 per cent diodrast solution (using the two-way stopcock). The

stopcock is opened to make sure the needle is still in the vessel and the contrast medium injected as rapidly as possible. The signal for exposing the film is given by the assistant making the injection at the moment when all of the dye has left the syringe (5 cc. remain in the tubing). The syringe is exchanged for another containing either citrate or physiological saline solution, and the needle and tubing kept patent by slow injection of the solution. Meanwhile, the roentgen technician removes the exposed plate, inserts another, and changes the position of the tube for a stereoscopic film. The second injection is now made. If a phlebogram is desired a third film is exposed, with a delay of four to six seconds between injection and exposure. Obviously, fewer injections and less total contrast medium would be needed with appropriate rapid plate changers.

It is usually possible to make some changes in the position of the patient's head and neck after the needle is in place without disengaging the artery. Therefore, if an anteroposterior view is desired, the plate holder is shifted and placed under the head (or the head moved onto the plate holder). The timing for film exposure is altered,* and the plate is exposed at the end of the injection just as with the lateral views. The position of the roentgen tube and the plate varies depending on the type of anteroposterior view desired. Axial, true anteroposterior and occipital views reveal different aspects of the vertebral circulation (Fig. 1d and 6c).†

It is possible to do carotid and vertebral angiography one after the other, especially in search of an aneurysm which cannot be localized clinically. Up to six injections (120 cc.) of diodrast have been used without harm. There is enough time between the two sets of injections to prevent overloading of the circulation with diodrast. Patients with obvious kidney damage have not been subjected to arteriography as yet and the limits of tolerance are unknown.

When the films have been made the needle is withdrawn from the neck and a gauze held over the puncture wound with firm pressure and taped into place. The anesthesia is discontinued, the patient extubated, and returned to his bed, where the usual post-anesthetic watch is kept. An ice collar may be applied to the neck for swelling and codeine given for pain when the patient awakens. Ordinarily, these inconveniences are not encountered.

Figure 1a demonstrates a normal vertebral arteriogram seen from the side. Almost inevitably, the petrous bone and mastoid air cells obscure much of the circulation, but the following vessels can be demonstrated. In the neck is seen the cervical portion of the vertebral artery, usually straight in the foramina transversaria to the level of C_2 where there is a bend in the transverse plane before the vessel passes laterally to go through the atlas. Emerging from the first cervical transverse process the vessel has another lateral bend before it enters the cranium. The course within the head follows the clivus, diverging from the bone at the dorsum sellae to divide into the terminal posterior cerebral arteries. Just after passing through the foramen magnum, the posterior inferior cerebellar artery can be seen arising with a convoluted first portion. Just before the posterior cerebral arteries are formed may be seen the superior cerebellar artery, paralleling the cerebral vessel in the first part of its course. The smaller vessels seen in the upper portions of the posterior fossa and in the region of the occipital lobes are branches of these larger vessels. Frequently, with proper timing (Fig. 2b and 5) a haze of small vessels can be seen arising from the basilar-vertebral system, running forward into the thalamus. The main vessels of this group are the posterolateral

* The technical data for these exposures are as follows: (a) Lateral exposures: 55 kv., 100 ma., 0.5 second. (b) Axial or occipital exposures: 75 kv., 100 ma., 1.25 second. The head unit was specially devised at the University of Chicago, and uses a G.E. tube, fixed tube-casette holder distance of 36 inches, and Potter-Bucky diaphragm.

† Because the rubber intratracheal tube is radiopaque, it is better to use a plastic intratracheal tube for angiography in case anteroposterior views are desired.

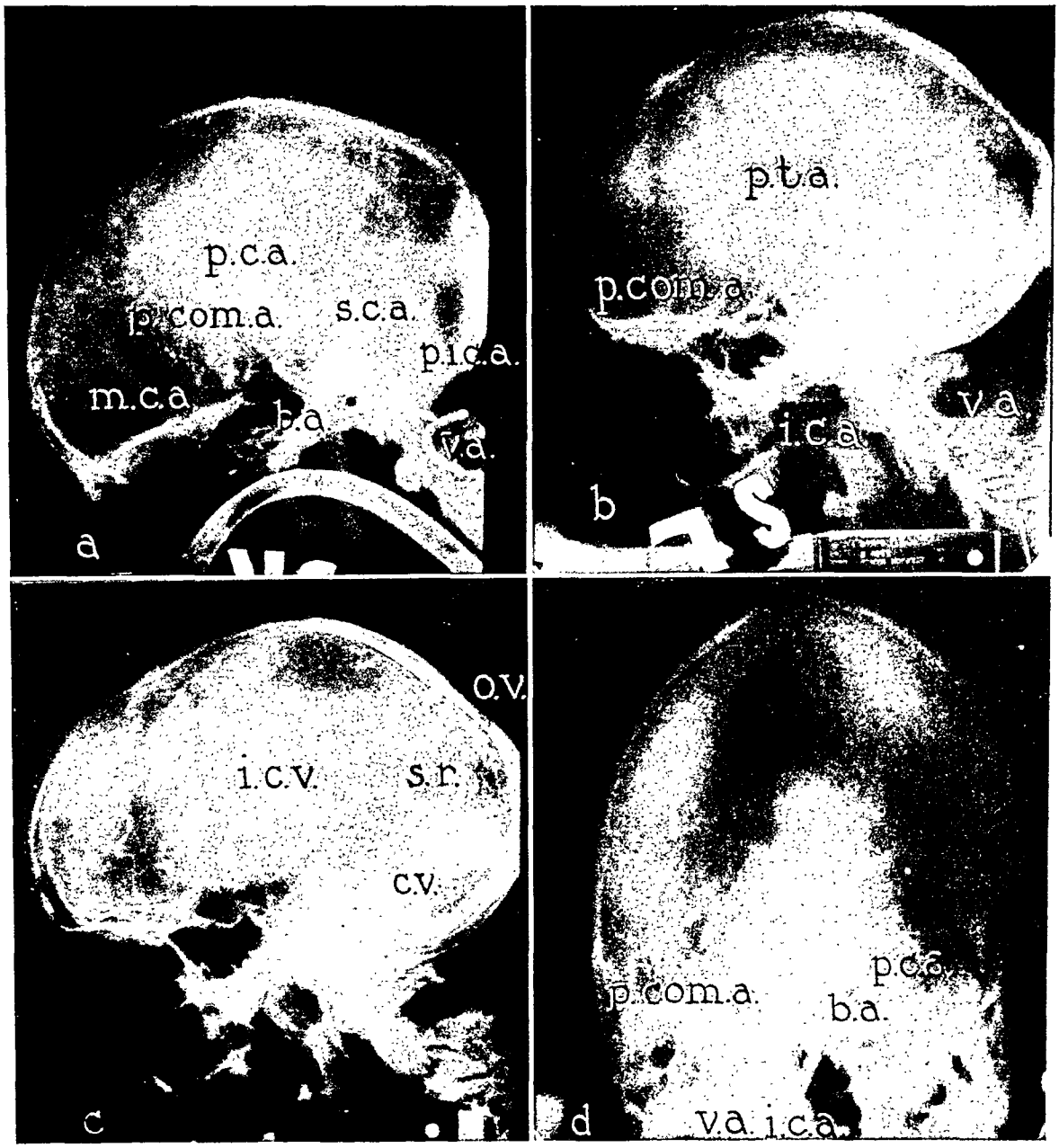


Fig. 1. Normal vertebral angiograms. (a) Normal vertebral arteriogram (lateral projection). (b) Normal vertebral arteriogram, with communication to the internal carotid artery. Note the needle point entering the vertebral artery. (c) Normal vertebral phlebogram. (d) Normal vertebral arteriogram (occipital view) showing, on left, communication with carotid system.

The following abbreviations are used for all the figures: *a*—aneurysm; *a.c.a.*—anterior cerebral artery; *b.a.*—basilar artery; *c.v.*—cerebellar veins; *i.c.a.*—internal carotid artery; *i.c.v.*—internal cerebral vein; *m.c.a.*—middle cerebral artery, *p.c.a.*—posterior cerebral artery, *p.c.v.*—posterior cerebral veins, *p. comm. a.*—posterior communicating artery; *p.i.c.a.*—posterior inferior cerebellar artery; *p.t.a.*—posterior thalamic arteries; *s.c.a.*—superior cerebellar artery; *s.r.*—sinus rectus; *v.a.*—vertebral artery.

(thalamogeniculate) and posteromedial (thalamoperforating) branches of the posterior cerebral artery. Occasionally, the posterior communicating artery and portions of the middle and anterior cerebral arteries may fill (Fig. 3b and 1a). Under circumstances as yet unclear, there is sometimes retrograde filling of an opposite vertebral artery (Fig. 5b); at other times there is filling of the internal carotid artery

(Fig. 6d) by reflux, apparently from the circle of Willis.

The venous return from the vertebral injection finds its way into the posterior cerebral cortical veins (which empty into the superior sagittal sinus) as well as into the internal cerebral vein and the straight sinus (Fig. 1c)

While a variety of other views of the vertebral-basilar system may be taken, the most valuable adjuncts to the routine lateral exposures appear to be the occipital and axial views. In the former (Fig. 1d) there is a somewhat blurred tree-like structure, showing filling of both posterior cerebral arteries and their branches in the cerebrum. The cephalad portion of the vertebral artery and the basilar artery can be seen, somewhat foreshortened. In this particular film, there arises from the left posterior cerebral artery a small short vessel passing downward to empty into a large artery which appears to pass further downward to cross the superimposed vertebral artery. These structures can also be seen in a lateral view (Fig. 1b) and almost certainly represent the posterior communicating and internal carotid arteries. The axial view (Fig. 6c) gives an excellent view of the basilar artery. The lateral pontine and other vessels which come off at right angles are not visible in this film. Occasionally, this view allows visualization of the reflux into the contralateral vertebral artery.

Figure 1b shows the tip of the needle in the vertebral artery and gives some idea of the angle of incidence.

The following case histories indicate some of the uses to which vertebral arteriography might be turned.

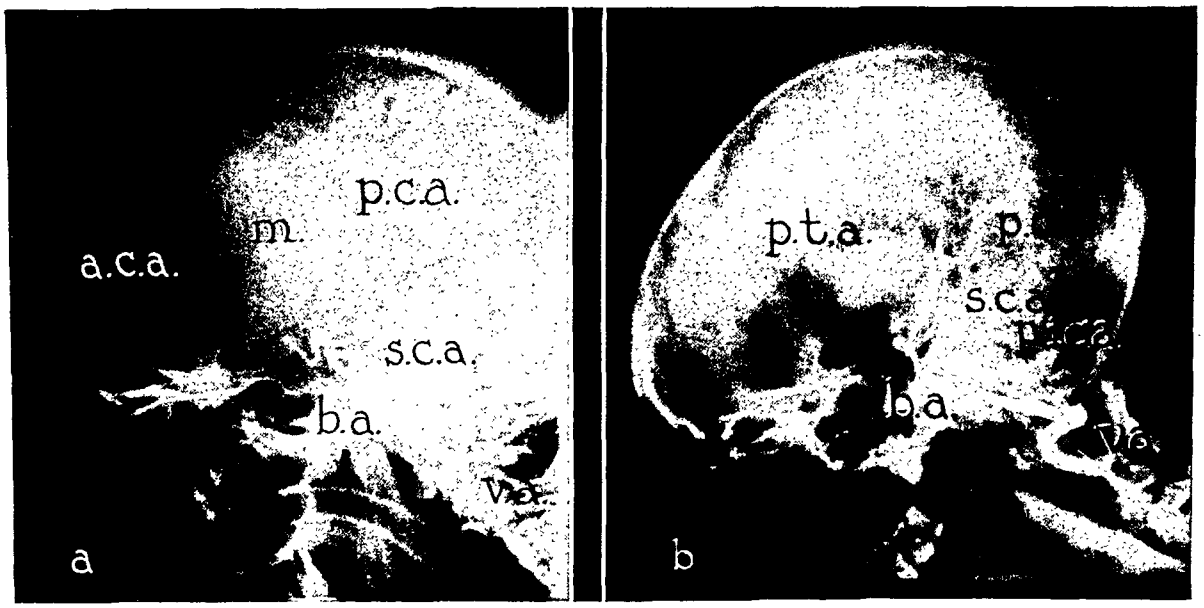


FIG 2. (a) Vertebral arteriogram showing thalamic metastasis (*m*). (b) Normal arteriogram showing the thalamic blood supply, for comparison with the vascularity of (a).

CASE 1. F. F. (Hosp. No. 107027), a white male laborer, aged forty-nine, was hospitalized because of occipital and frontal headaches, numbness and weakness of the left arm and difficulty in walking, all of two weeks' duration. He had been constipated for years and five months prior to hospitalization had had bloody stools for two or three days. Occasionally nausea was present during the development of his neurological symptoms.

Examination on August 28, 1946, revealed some dullness on percussion at the left lung base, musical wheezes at the left apex, and expiratory wheezes over the right upper lung. The abdomen appeared normal, and no peculiarities were found on rectal examination.

Neurological study showed dilatation of the right pupil, bilateral blurred disc margins, hemiparesis on the left with hyperactive tendon

reflexes, incoordination of arm and leg movements, and falling to the left in Romberg's position and in walking. There was a questionable Babinski sign on the left. Routine blood count, serology, chemistry and urinalysis were not revealing. Roentgenograms of the chest were reported as indicating an old healed tuberculosis with densities suggestive of metastatic malignancy.

On September 3, 1946, a right carotid angiogram was attempted. When the films were developed (Fig. 2a), it was seen that the cerebral circulation was injected by way of the vertebral artery. Most of the vessels of the posterior fossa are obscured. The anterior half of the basilar artery is seen, branching to give off the right superior cerebellar and posterior cerebral arteries. The posterior communicating artery is filled, and shadows of both anterior cerebral arteries are seen, one definitely anterior to the other. Arising from the region of the basilar termination is a single vessel passing upward to the region of the thalamus, where it breaks up into a circumscribed circular mass of minute blood vessels. On September 6, 1946, a right fronto-temporo-parietal bone flap was turned down revealing tense dura mater but with considerable fluid in the subarachnoid space. Then parietal and temporal areas were needled, but no tumor was encountered. A decompression was left, the temporal horn filled with air, and films taken later which showed shift of the third ventricle to the left, with the occipital horn on the right in good position. Postoperatively there was left hemiplegia. Roentgen therapy was begun on the sixth postoperative day, but the patient developed bronchopneumonia and died on September 17, 1946.

Autopsy revealed bronchopneumonia, old healed tuberculosis of the lungs, and carcinoma of the rectum with metastases to the regional nodes, cecum, spleen, kidney, adrenals, pancreas, stomach, lungs and brain. Sections through the brain showed metastases in the right frontal and parietal lobes, left cerebellar hemisphere, pons, and there was a metastasis (3 cm. in diameter) in the right thalamus, pushing the internal capsule to the right. This is undoubtedly the mass shown in the arteriogram in Figure 2a. Microscopic study showed adenocarcinoma.

Case II. W. H. was only five years old when he fell while holding an open knife, the blade entering his left lower lid. There was bleeding from the wound, and protrusion and edema of the orbital contents. Vision was not impaired. The swelling fluctuated intermittently, until at the age of eight he was struck again in the eye, causing an increase in swelling. This progressed during the next two years. He was examined at

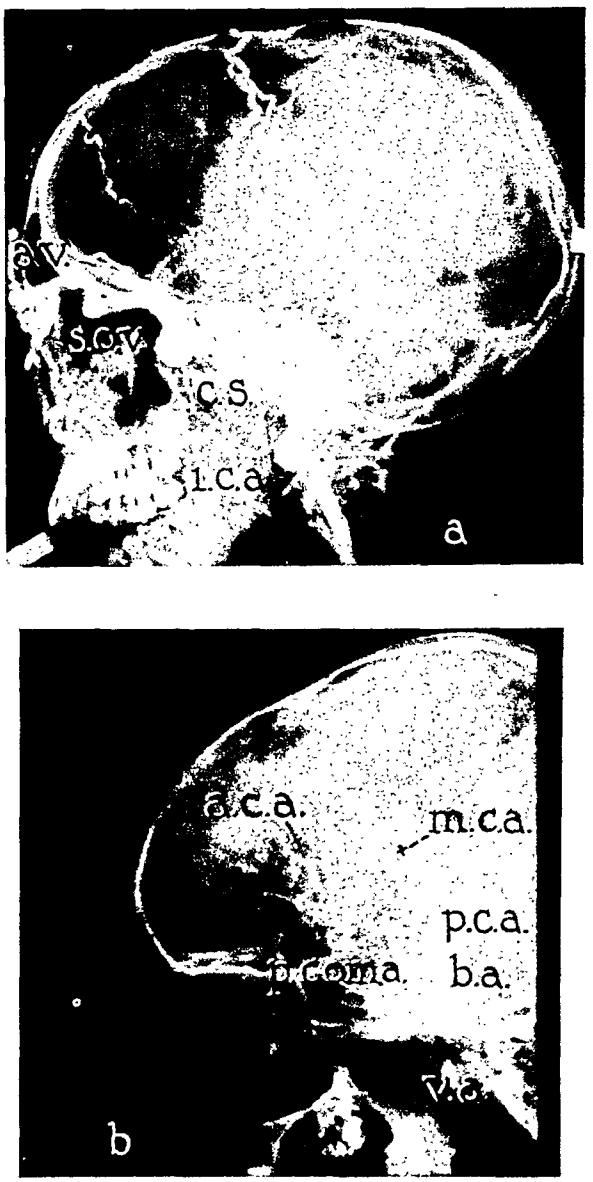


Fig. 3. Case II. Carotid-cavernous fistula. (a) Carotid arteriogram. *c.s.*—cavernous sinus; *s.o.v.*—superior ophthalmic vein; *a.v.*—angular vein. (b) Vertebral arteriogram.

the age of ten at the Illinois Eye and Ear Infirmary, where a diagnosis of pulsating exophthalmos was made. He was transferred to the Illinois Neuropsychiatric Institute (Hosp. No. 112177).

Examination of this ten year old colored boy showed protrusion of the contents of the left orbit with a pulsating mass in its superior portion. A bruit could be heard here. The left side of the forehead was crossed by tortuous dilated blood vessels, compression of which caused swelling of the left orbital contents. The angular vein was especially prominent. The conjunctiva of the left eye was engorged. Vision was 20/20 in each eye. Because it was impossible to tell which vessels were involved arteriography was suggested. On June 20, 1947, diodrast was injected into an artery in the neck in an attempt to do carotid angiography. Roentgenograms showed (Fig. 3b) filling of the vertebral and basilar system, with marked dilatation of the communicating vessels allowing filling of the anterior cerebral and middle cerebral arteries. Because of difficulty in finding the carotid artery, the boy was taken to the operating room where the carotid vessels were surgically exposed; he was then returned to the Roentgen Department where the common carotid artery was injected with diodrast. The films now taken showed (Fig. 3a) filling of the internal carotid artery as far as the sella turcica. Here the contrast medium is seen to pass into the cavernous sinus and the superior ophthalmic vein and out into the facial and angular veins to fill (ultimately) the superficial temporal and frontal veins. It was then clear that this was a classical traumatic carotid-cavernous fistula and that there was adequate circulation for the anterior half of the brain through the basilar system. On June 24, 1947, both the internal and the external carotid arteries on the left were again exposed and separately ligated, causing disappearance of the bruit, thrill and pulsation. The next day there was again some slight thrill and bruit over the eye, but this was no longer evident in the forehead. The boy was sent home on the eighth postoperative day. He was seen last on March 18, 1948. There was still a slight proptosis with mild bruit audible over the eye. This could be obliterated by compression of the right (contralateral) common carotid artery. There was no evidence of glaucoma and no visual disturbance. He had no pain and it was agreed that no further therapy was needed, at that time.

CASE III. S.Mc., a housewife, aged fifty-two, was a known diabetic for over a year. She was also known to have benign essential hypertension. Three weeks before hospitalization she began to vomit several times a day, had some difficulty in talking, was unable to walk, and gradually lost urinary sphincter control.

Examination on admission on March 20, 1948 (clinic No. 339047) revealed blood pressure of 160/110. The heart was enlarged to the left and electrocardiogram showed an abnormal tracing compatible with chronic cardiac disease. Other than an arteriovenous ratio of 1:2 in the fundi, there were no signs of arteriosclerosis. There was mild nystagmus on lateral gaze. Hypalgesia of the cornea and face on the right and of the left side of the body below the face was present. Mild hemiparesis with spasticity was found on the right side, including a right central facial weakness. The tendon reflexes on the right were increased and the Hoffman's and Babinski's sign were present on the right. Spinal puncture revealed no abnormalities of pressure but the protein was slightly elevated to 50 mg. per cent. Because of the bilaterality of symptoms, arteriography was suggested.

On April 2, 1948, the right vertebral artery was injected percutaneously with diodrast and roentgenograms taken (Fig. 4). The vertebral and basilar arteries are quite narrow compared to normals (Fig. 1b and 2b), and the acute bends of the normal vessels are opened out. There are irregularities of diameter of the extracranial portion of the vertebral artery. The intracranial branches are sparse and the



FIG. 4. Case III. Vertebral-basilar arteriosclerosis. Note narrowed and irregular contours compared with those of Figures 1, 2b, 3b.

terminal vessels exceedingly tenuous. These findings are considered to be compatible with arteriosclerosis of the vertebral-basilar system.

During the next few weeks the hypalgesias diminished, the right hemiparesis grew less, a right Horner's syndrome appeared, only to disappear again by the time of discharge. The diagnosis at discharge was encephalopathy due to brainstem arteriosclerosis.

Case iv. E.B., a housewife, aged thirty-eight, had severe headaches and stiff neck following the birth of her second child five years before she was hospitalized. She was otherwise well until October 7, 1947, when she was found comatose and moaning in the bathroom. She was taken to another hospital where spinal fluid pressure was 400 mm. water and numerous red blood cells were found in the fluid. Punctures were repeated twice daily and she improved, talked, and her headaches diminished. She was transferred to the Illinois Neuropsychiatric Institute (clinic No. 334325) on October 22, 1947. There was some residual nuchal rigidity and there was weakness of the left lower face and left leg, with absence of abdominal reflexes on that side. There were Babinski's signs on both sides. She seemed to be somewhat dull and confused. Lumbar puncture pressure was 170 mm. of xanthochromic fluid with positive Pandy's test and no cells, and with 96 mg. per cent total protein. Skull and chest films and routine laboratory studies were normal. On October 25, right cerebral angiography was done by the percutaneous technique under pentothal anesthesia; no vascular anomaly was disclosed. On October 29, angiography of the left common carotid artery similarly proved to be normal. Two days later, while expelling a bowel movement, she had a seizure followed by Cheyne-Stokes respiration and coma. Lumbar puncture yielded bloody fluid at a pressure of over 600 mm. water.

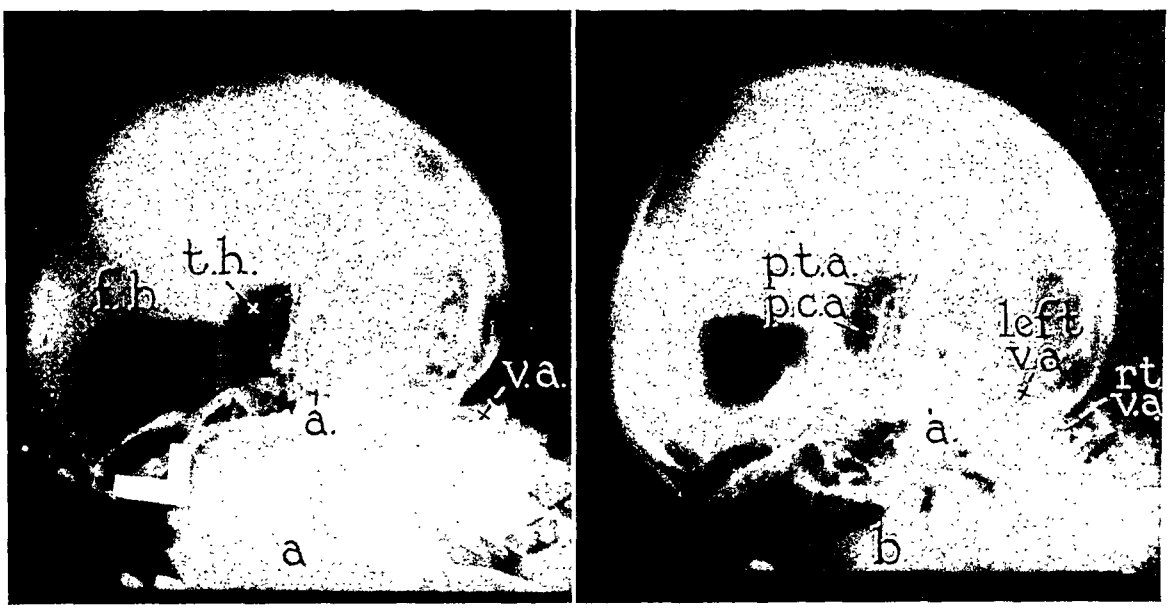


Fig. 5. Case iv. Basilar aneurysm (E.B.). (a) *f.h.*—frontal horn; *t.h.*—temporal horn. (b) Stereoscopic view, showing both vertebral arteries. The aneurysm is less clearly disclosed below the auditory meatus.

Fifteen cubic centimeters were removed slowly, reviving the patient, who began to cry with headache. Later, electroencephalography was done, showing diffuse irregular slowing in all leads, with some 4–7 per second activity in only the left hemisphere. In the ensuing days she became more lucid and complained less. On November 17, neurological study showed slight lower left facial weakness. Air conduction was not now better than bone conduction on the right, and Weber's test lateralized to the right. The left abdominal reflex was depressed. Aside from some confusion there were no other neurological signs. She began to become irrational. Because of the possibility that the bleeding might be from a tumor not previously visualized and because the angiograms showed upward curving of the callosal arteries, pneumoencephalography with helium was done under

pentothal anesthesia. The films showed generalized dilatation of the ventricular system without filling of the subarachnoid spaces. She became more and more confused and had to be sedated with paraldehyde. On November 25, 1947, it was decided that vertebral angiography should be done. This was done, for the first time deliberately, by the percutaneous method. Stereoscopic films (Fig. 5a and 5b) show residual gas in the tips of the dilated anterior and temporal horns. Posterior to the dorsum sellae is seen a bilobed mass at the level of the acoustic meatus, continuous with the basilar artery both anteriorly and posteriorly. The posterior cerebral artery crosses the gas shadow in the temporal horn and above this can be seen the filagree of fine thalamic vessels. In Figure 5b both vertebral arteries can be seen, indicating reflux from the basilar artery. Stereoscopic visualization clearly indicates the dilatation is in a portion of the basilar artery. It was decided that this lesion would not be amenable to surgical attack.

In the fortnight which followed, she was irrational, incontinent, and had to be spoon fed. She gradually improved, could sit in a chair, became continent and more coherent, and was discharged on December 9, 1947. She was most recently seen in the out-patient clinic on May 13, 1948. She had been walking but with difficulty. She complained of mild headache and pain over the left eye. There was spasticity and increased reflexes on the left and some left lower facial palsy. Bilateral Babinski's signs persisted. She was eating well and seemed content.

CASE V. C.W., a white housewife, aged forty-one, was admitted to the Illinois Neuropsychiatric Institute (clinic No. 337105) for evaluation of intracranial pathology on January 26, 1948. Five years earlier, she had had a dizzy spell, had fallen, but was not unconscious. Strabismus was found. Lumbar puncture was reportedly normal. After two weeks she recovered and remained well for the next two years except for frequent headaches. She then had sudden onset of unconsciousness which lasted for six hours and lumbar puncture yielded bloody fluid. During the next thirteen weeks she had repeated episodes of unconsciousness, confusion, disorientation, with urinary incontinence and right-sided paralysis. She gradually regained the use of her sphincters and had sufficient recovery to be able to walk with assistance. Difficulty in speaking arose about this time but it also improved. Three months before admission the right-sided weakness returned with urinary incontinence and increase in speech difficulties. There were also frequent outbursts of crying.

Examination revealed a marked spastic hemiplegia with hyperactive tendon reflexes, Babinski's sign and absent abdominal reflexes on the right. The left lower extremity was also weak, with exaggerated deep reflexes, ankle clonus and Babinski's sign. There was bilateral tremor at rest. The left pupil was larger than the right but reacted well to light and in convergence. The extraocular muscle movements were normal. She was unable to speak when excited and was easily moved to tears or laughter, often inappropriately so. Blood counts, blood chemistry, serology, urinalysis and plain skull films were normal. Electroencephalogram showed a mildly slow record with no evidence of localized disorder in the accessible cortex. On January 29, 1948, a left carotid arteriogram was attempted, but fortunately the left vertebral artery was injected instead. This revealed (Fig. 6a) a huge aneurysm at the end of the basilar artery. The circulation appeared otherwise normal. Study of the stereoscopic arteriograms and of the phlebogram (Fig. 6b) failed to reveal the exact point of origin of the outpouching. It was felt that a carotid angiogram might shed some light on this. This was done by the percutaneous method on the left side on February 4, 1948. The intracranial circulation appears (Fig. 6d) normal except that the first portion of the left posterior cerebral artery and posterior communicating artery is pushed upward leaving a large clear space behind the sella turcica which corresponds well to the region of the aneurysm. The patient recovered readily from this procedure and was discharged on February 13, 1948, in care of her family.

In later reviewing this case it was felt that there was a remote possibility that the neck of the aneurym might be clipped. The patient was, therefore, readmitted on April 3, 1948. She lay in bed, unable to control her emotions and displayed pathological laughing and crying. There was dysarthria, right hemiparesis with increased tendon reflexes, clonus and Babinski's sign. There was increased tendon reflex activity in the left leg with clonus and Babinski's sign. Sensation was intact. The left pupil was larger than the right. Anteroposterior vertebral angiography had been requested to visualize more clearly the point of origin of the aneurysm. On

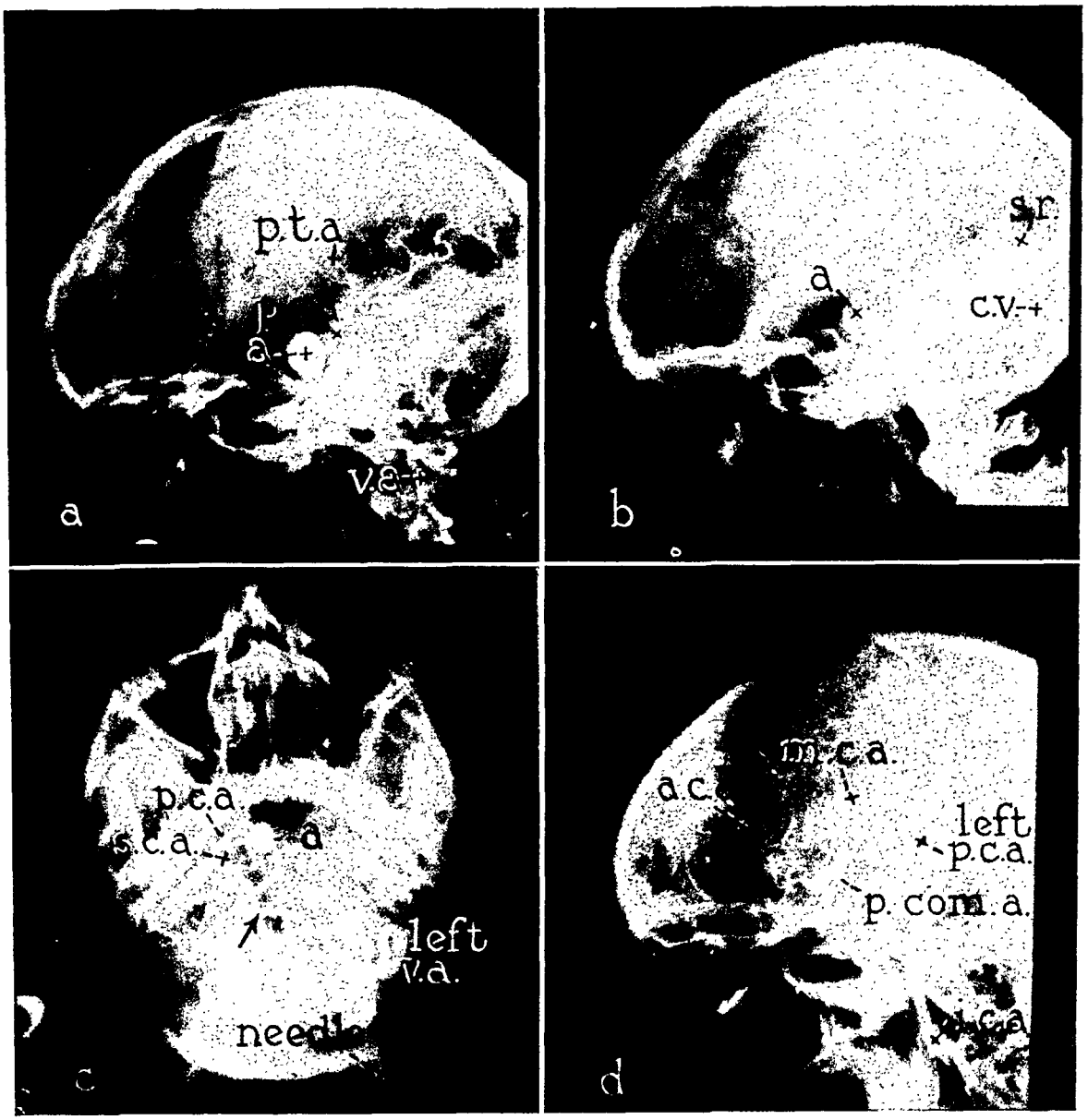


Fig. 6. Case v. Basilar aneurysm (C.W.). (a) Vertebral arteriogram (lateral view). (b) Phlebogram, with dye still in aneurysmal sac. (c) Vertebral arteriogram (axial view). The arrow marks the site of junction with the right vertebral artery, not shown in this film. (d) Carotid arteriogram (lateral view) Note pushing upward of first portion of left posterior cerebral and posterior communicating arteries.

April 10, 1948, the left vertebral artery was deliberately injected percutaneously with the patient's head lying on the plate holder in such a way that an axial view could be taken. To avoid excessive shadow, a plastic intratracheal tube was used instead of the conventional rubber tube. Because of the density of the basal structures, it was felt expedient to use thorotrast (12 cc.) for one, and diodrast for the other of the stereoscopic films. Both gave good contrast. Figure 6c shows the needle entering the left vertebral artery which is convoluted where it enters the skull. The basilar artery is of a reversed S-shape and at its terminus is the rounded aneurysm, from which arise the posterior cerebral and posterior cerebellar arteries of the right side. In the stereoscopic plate (which is not shown) the cephalad 2 cm. of the right vertebral artery is also filled, by reflex.

It was then apparent that there was little to be done in the way of therapy. The following morning the patient rather rapidly became cyanotic and restless but not confused, and was able to ask for water. The left pupil was more

dilated. The blood pressure gradually fell, the temperature rose and the pulse became weaker. Lumbar puncture revealed clear colorless fluid with 80 mm. fluid pressure, no cells, and negative Pandy's reaction. Rales developed in both lungs in spite of oxygen and chemotherapy and she died in the morning of April 13, 1948.

Autopsy revealed extensive bilateral bronchopneumonia. Gross examination of the brain

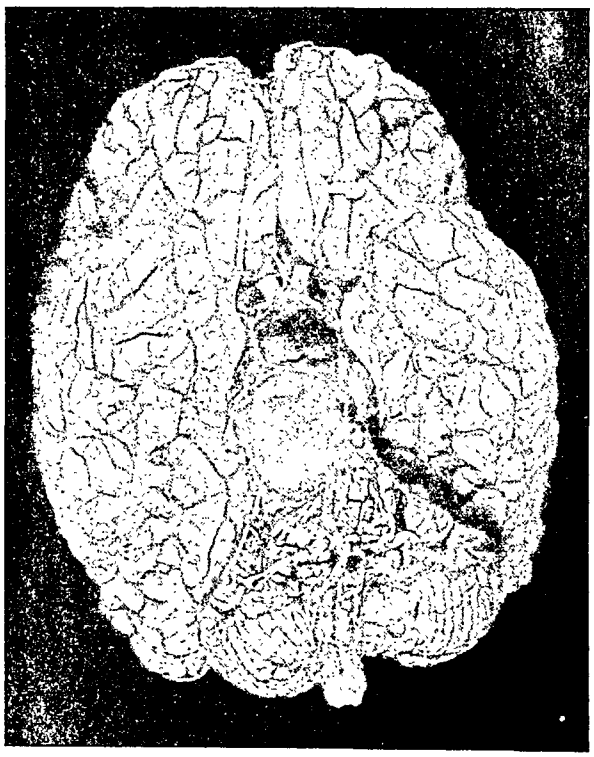


FIG. 7. Case v. Basilar aneurysm (C. W.). Photograph of base of brain at autopsy showing aneurysm.

revealed a firm rust-colored walnut-shaped mass about 3 cm. in diameter (Fig. 7). It lay anterior to and tended to compress the more cephalad portion of the pons, which in turn surrounded the posterior superior surface of the mass. Rostrally, the lesion extended to within 5 mm. of the pituitary stalk. The basilar artery entered slightly (2–3 mm.) to the right of the middle of the lesion. About 1 cm. to the right of this point of entry there was another artery which appeared to arise from the bulbous mass and immediately divided into the posterior cerebral and anterior superior cerebellar arteries. Also arising at this point was a thin band of tissue which traversed the right side and anterior aspect of the mass to reach the posterior communicating artery on the left, about 1 cm. posterior to the origin of the left optic tract. A probe passed up the basilar artery entered the terminal mass. The entire region has been kept as a gross museum specimen, so sections are not available.

DISCUSSION

Although Egas Moniz[19] introduced carotid angiography in 1927, he was loath to inject the vertebral arteries because of the physiological importance of the medulla oblongata and because of the difficulty in exposing the vertebral artery. When, in 1933,[20,21] he compiled data from 600 arteriograms in his files, he noted 5 cases in which the basilar, posterior cerebral, and even cerebellar arteries were filled. Moniz thought this occurred by retrograde filling down the carotid into the subclavian and vertebral arteries. In none of the figures presented in his monograph of 1940[19] is the cervical portion of the vertebral artery seen, although the basilar and carotid systems are well filled. It seems much more probable that the flow was through the posterior communicating vessels (see also Fig. 1b). None of these patients was injured by the procedure, so it was felt safe to investigate the posterior fossa deliberately. Direct vertebral exposure and injection appeared to be too difficult and uncertain, so Moniz, Pinto and Alves[21] introduced the technique of retrograde injection into the subclavian artery. This vessel was exposed by incision parallel to and above the clavicle. Injection of 14 cc. thorotrast was made against the flow after temporary occlusion of the peripheral part of the vessel. This allowed visualization of the carotid and vertebral vessels on the right, and of the vertebral on the left. His figure 87 (1940)[19] shows upward displacement of the superior cerebellar and posterior cerebral arteries by a posterior fossa tumor.*

Olivecrona (1935)[22] succeeded in injecting the exposed vertebral artery directly. Berczeller and Kugler[1] described a technique based on cadaver dissection, with injection of the vertebral artery as it passes

* This is the same figure as is shown in the articles in 1933[20,21] with Pinto and Alves. The displacement is not marked in the reproductions and is not as impressive as that of Shimidzu's case.[27]

from the transverse process of the atlas. They suggested that the artery could be injected at this locus at the time of suboccipital exploration; films taken in the operating room could then be used for orientation of the operator.* Unfortunately, no clinical examples are given, nor is there evidence that this operative approach was used in a living patient.

Shimidzu (1937)[27] was successful in injecting the subclavian artery percutaneously in a modification of Moniz's idea of retrograde filling of the vertebral artery.† Sjöqvist[28] was dissatisfied with the results of retrograde filling, but with direct exposure of the vertebral artery at its entry into the transverse process of C_6 he had better success. In each of 8 instances, 10 cc. of thorotrast were injected, with good filling in 6 cases. Three of these were normal. One showed displacement of the basilar artery in a case of cerebellopontine angle tumor. This could not be considered diagnostic, however, for in another case of similar displacement operation failed to disclose a tumor and it was concluded that the marked curvature might well be an anatomical variation. In the last case, ventriculogram indicated tumor of the fourth ventricle in a seven year old boy. At operation no tumor was seen, but a vessel between the tonsils was interpreted as a vascular malformation. An arteriogram appeared to confirm this and the vertebral artery was tied off in the neck. Symptoms recurred and reoperation revealed medulloblastoma. Eventual autopsy disclosed no signs of vascular malformation.

In 1940, Takahashi[29] described a percutaneous technique for vertebral injection, apparently done under local anesthesia. A horizontal line was drawn 4 cm. below the thyroid incisura. Where the carotid pulsation crossed this line was taken as a point overlying the vertebral artery. A line was drawn from here to a point on the clavicle 2 cm. lateral to its inner end, and this line was taken as the line of the vertebral artery. A needle attached to a syringe was inserted over this line and, at a depth of 3.5–4.5 cm. the artery could be encountered and recognized by blood pushing into the syringe. Four to 5 cc. of thorotrast were injected and lateral or anteroposterior films taken immediately. This procedure was felt to be without danger, although more difficult than percutaneous carotid arteriography. Irritation of the vagus to cause vomiting is the only complication mentioned. A vertebral arteriogram is shown which has filling of the entire intracranial circulation in a woman, aged twenty-eight, with complete occlusion of the common carotid arteries from thromboangiitis obliterans (proved by biopsy and autopsy findings.)

This percutaneous technique was thought by Krayenbühl (1941)[12] to be too complicated and uncertain, so he used Moniz's open subclavian retrograde technique. A case of aneurysm at the junction of the posterior cerebral and posterior communicating vessels is described, and the arteriogram shown. In this case, carotid angiography had failed to disclose the vascular abnormality responsible for left oculomotor palsy and subarachnoid hemorrhage in a forty-five year old man.

The first reported instance of vertebral angiography in the United States is that of King (1942),[11] who injected 10 cc. of thorotrast into the exposed vertebral artery, using a right-angled needle. The patient, aged forty, had subarachnoid bleeding complicating central nervous system syphilis. A bulbous end was thought to be disclosed at the cephalad tip of the basilar artery, and it was speculated that this might be an aneurysm (actually it is a normal configuration; see Figure 2b for a comparable finding).

* This has been done successfully by Dr. A. Ecker of Syracuse (personal communication).

† The needle was inserted through the omoclavicular trigone towards the palpable pulsation of the subclavian. The injection of 7–8 cc. of thorotrast was made after an assistant occluded the axillary artery in the axilla. Figures are shown of increased vascularity having its origin in a superior cerebellar artery in a thirty year old male with a meningothelioma under the right tentorium and of pushing upwards of the posterior cerebral artery and basilar artery tip by a pontine tumor in a nineteen year old male. In both of these autopsy confirmed the vascular changes in the tumor.

The long dearth of reports during World War II ended with that of List, Burge and Hodges in 1945.[15] They used Moniz's technique for vertebral visualization in 6 patients during the three year period covered by their paper. Tracings of the vessels are shown, but no reproductions of films or cases reported. List (1946)[14] was dubious about percutaneous vertebral angiography because of the small size and deep position of the vessel. In the discussion of this paper, Freeman[7] mentioned visualization of the vertebral circulation by injections made through skin puncture.*

Lowman and Doff[16] still considered (1945) open techniques the only possible means for introduction of contrast medium into the vertebral-basilar system. Poppen (1948)[24] used the Moniz technique for vertebral angiography but mentioned percutaneous injection into the subclavian artery when this arched high above the clavicle.

Radner† has described a technique in which a rubber catheter is inserted into the radial artery and moved under fluoroscopic control until the tip is opposite the opening of the vertebral artery. Diodrast is then injected to obtain a vertebral angiogram. This entails sacrifice of the radial artery, but this is considered of little consequence in view of the rich collateral circulation at the elbow.

It appears to us that the percutaneous technique described above is simpler and less liable to error than that of Takahashi. It offers the usual advantages of a percutaneous technique—lack of operative procedure, ease of repetition, less total time consumed, as well as the usual disadvantages of a "blind" injection—extravasations of contrast medium, invisible hemorrhages, difficulty in finding the vessel. Even the open methods are not always productive of good end results (Sjöqvist). In experienced hands by the percutaneous method the probability of obtaining good visualization is high. We have not attempted to make these injections under local anesthesia, although this could be done after infiltration of the regions involved, just as percutaneous carotid arteriograms have been done. The experience is doubtless a distressing one and, in the past, we have found it preferable to do carotid angiograms under general anesthesia (after having tried them under local anesthesia as well).

In the more than 20 successive deliberate vertebral angiograms done here, failure to fill the vertebral artery has occurred only twice. In each of these early attempts, the failure was due to lack of appreciation of the venous character of the blood entering the observation tube. It did not rush back into the tube and had to be aspirated. In each case injections were made and films exposed. In each, the vertebral veins and their cervical tributaries are seen. Since then, injections have not been made until bright red blood with good pressure has pushed its way into the syringe-needle system.

There have been two instances of urticarial reaction to diodrast following the injections, in spite of absence of reaction to an intravenous test dose of 5 cc. These responding readily to ephedrine sulfate. Extravasation of diodrast due to improper placement of the needle or movement of the patient has occurred. This has caused no great difficulty and later roentgenograms show the dye is soon taken up from the extravascular tissues. There have been no hemorrhages or hematomas recognized, although these might well be present and not disclose themselves.

One patient subjected to vertebral angiography as a part of a complete diagnostic survey for intractable headache, developed a brachial plexus root neuralgia. During the needling for the artery in this early case, the needle was passed lateral to the transverse process in attempting to find its tip; it was also passed caudally from its locus on the bone in attempting to find the artery below the transverse process. In so manipulating the needle, it was obvious that a

* He states (1938, personal communication) that these were not deliberate vertebral injections.

† Radner, S. Intracranial angiography via the vertebral artery. Preliminary report of a new technique. *Acta radiol.*, 1947, *38*, 838–842.

nerve root had been struck, for there was twitching of the deltoid muscle. The complaints of the patient postoperatively seem to be out of proportion to the trauma and it is possible that a large psychogenic factor is exaggerating the neuropathy. Since this time, however, it is considered unwise to direct the needle caudally in trying for the vertebral artery. Actually we have found it is more difficult to inject the artery low in the neck and our best and easiest injections have been made above the fifth cervical transverse process. By always passing the needle in a cephalad direction, one is less likely to strike the cervical nerve roots which are given some protection by the superior anterior ledge of the transverse process.

It is theoretically possible to enter the intervertebral foramen by directing the needle point sufficiently medially. This might engage the spinal nerve, the root sleeve, or even enter the spinal canal. This is avoided by proper direction of the needle tip.

It is also possible theoretically to produce a traumatic arteriovenous fistula in the vertebral canal by puncturing both vessels. There is no evidence that this has occurred in any of these patients. In the presence of normal clotting mechanisms and with a sharp needle, the holes in the artery and vein (if both be injured) should close over quickly (especially since the direction of the puncture into the artery favors automatic closure by pressure from within).

One as yet unexplained complication has recently been encountered. It brings to mind the occasional instance of hemiparesis which may follow carotid angiography.

Case vi. B.R., a farmer, aged forty-one, had severe frontal headaches for a week, starting December 24, 1947. These receded with treatment for sinusitis, but on January 1, 1948, he had an intense frontal headache, blurring of vision, and a major seizure followed. He was unconscious and incontinent three hours later and removed to a hospital the next day. Here lumbar puncture revealed bloody fluid. He was irrational for several days but had no focal signs. Within three weeks he gradually recovered and was sent home. Here he soon regained his former strength but had such a mental depression that he was sent to the Illinois Neuropsychiatric Institute (clinic No. 340839).

He was admitted for arteriography, which was initiated two days after admission (after routine examinations and laboratory studies revealed no abnormalities). A right carotid arteriogram on May 7, 1948, failed to reveal any aneurysm. On May 12, a left common carotid and a left vertebral arteriogram were done without difficulty; they also failed to disclose an aneurysm or other vascular malformation. When he awakened from the anesthetic the next morning it was noticed that he had weakness (but not paralysis) of the left side of the body, diminished ability to perceive pinprick on the right half of the body below the neck and urinary retention. Lumbar puncture two days later yielded clear colorless fluid under normal pressure and with only 39 mg. per cent total protein. No red blood cells were seen. Over the course of the next few weeks the tidal drainage which had been instituted for the overflow incontinence was removed, strength began to return in the arm and leg, and the patient was able to be up, first with a cane and later without. He still had some unsteadiness in walking when he was discharged on June 20, 1948, to be allowed to continue convalescence at home.

Reviewing the technique of angiography in this case, we are certain that there was no maldirection of the needle into the spinal canal; no spinal fluid was obtained at any time, no blood was found in the spinal fluid, and there had been no unusual difficulties in finding the vertebral artery. The cause of the original subarachnoid hemorrhage has not been disclosed, nor can we ascribe a credible reason for the receding Brown-Sequard syndrome. That the vertebral angiography seems to be at the bottom of this appears to be certain, however, since the supposed site of the lesion is below the pyramidal decussation on the side of the angiography.

Visualization of the vessels of the posterior fossa has been considered of varying desirability by different authors. Sjöqvist (1938)[28] felt it was indicated for vascular malformations and vascular tumors. He thought it less useful than clinical examination and ventriculography for accurate

location of tumors of the posterior fossa. Moniz (1940)[19] was uncertain about its value, and thought it much less important than carotid angiography. He believed it useful for localization of cerebellopontine angle neoplasms (by lateral displacement of the basilar artery in anteroposterior views) and for angiomas and aneurysms of the posterior fossa. He found the vascular pattern of the tumors only rarely shown by vertebral arteriograms. Krayenbühl (1941)[12] felt that arteriography was valuable mostly for diagnosis of aneurysm and arteriovenous malformations. List (1946)[14] stated, "The diagnostic results of vertebral arteriography, however, are comparatively meager in comparison to the effort one makes to show the vessel." On the other hand, Shimidzu (1937)[27] remarked, "Bei schwerdifferenzierbaren Tumoren der Hinterschädelgrube ist die Arteriographie der A. vertebralis unentbehrlich. Es hilft vor allem zur Seitendiagnose, die für Operation wertvoll ist."* One gathers the impression that the value of this type of angiography rises with ease of performance and wide application in more cases.

Actually, the major use to which vertebral angiography has been put in our experience has been in the discovery of vascular lesions of the posterior fossa.

Aneurysms of the vertebral and basilar arteries have been known even before Cruveilhier (1835)[3] pictured a saccular aneurysm of the right vertebral artery. McDonald and Korb[17] refer to aneurysms of the posterior communicating arteries described by Morgagni in 1769 and to basilar artery aneurysms described by Blackall in 1814 and Hodgson in 1815. There have been several comprehensive reviews of intracranial aneurysm (McDonald and Korb, 1939[17]; Richardson and Hyland, 1941[25]) and isolated reports since then. Krayenbühl[12] described 2 aneurysms of the basilar artery and one of the left superior cerebellar artery disclosed at autopsy. These are in addition to the one disclosed by vertebral angiography to be at the junction of the posterior communicating and posterior cerebral arteries. Mitchell and Angrist[18] found 8 aneurysms of the posterior circulation (3 basilar, 2 vertebral, 1 posterior communicating, 1 posterior cerebral, 1 anterior inferior cerebellar artery) among 36 aneurysms found in 3,080 autopsies. Hoge (1943)[10] describes the case history and autopsy findings in an unruptured fusiform aneurysm of the basilar artery, due to arteriosclerosis. A rare fusiform aneurysm of the left posterior inferior cerebellar artery due to rheumatic disease is detailed by Lindsay (1944).[13] In Yaskin and Alpers' case (1944),[31] a large aneurysm of the left vertebral artery had compressed the cerebellum and brainstem, simulating a posterior fossa tumor. Dimitri and Aranovich (1944)[5] reported a rare aneurysm of the right superior cerebellar artery, ascribed to trauma.

Fattovich* discussed at some length the difficulty in diagnosis of one massive and one tiny aneurysm of the posterior communicating artery: the first occurred in a woman thought to have a basal tumor, and the other in a woman of sixty-one who appeared to have had an ordinary cerebrovascular accident. In neither of the 2 cases of aneurysm of the vertebral artery described by Rigdon and Allen† were there antemortem indications that the subarachnoid hemorrhage came from a vessel in the posterior fossa. From the pictures of the specimens, it appears that one, at least, might have been successfully attacked surgically.

In Dandy's[4] monograph of intracranial arterial aneurysms, 23 of 133 aneurysms are described as occurring on the posterior cerebral, basilar and vertebral arteries. Eleven of the basilar-vertebral group of 21 were discovered at operation; the rest, at autopsy. Poppen (1948)[24] states that 25 per cent of intracranial aneurysms occur in the posterior third of the circle of Willis and its

* "Arteriography of the A. vertebralis is indispensable in posterior fossa tumors which are difficult to differentiate. Above all it is a help in lateralization, which is valuable for operation."

* Fattovich, G. Contributo allo studio degli aneurismi intracranici. *Note e Riviste di Psychiat.*, 1940, *69*, 433–4621.

† Rigdon, R. H., and Allen, C., Jr. Aneurysms of the vertebral arteries; a consideration of their etiology. *J. Lab. & Clin. Med.*, 1944, *29*, 28–36.

vertebral flow. One patient with basilar aneurysm whom he reports had cranial nerve signs and typical glossopharyngeal tic. Two others in his series had vertebral aneurysms. Six of 46 autopsy confirmed aneurysms in Hamby's (1948)[9] series were on the basilar segment of the circle of Willis (posterior communicating, posterior cerebral, posterior inferior cerebellar and basilar arteries). Schwartz (1948)[26] has reported what appears to be the first arterial aneurysm in the posterior fossa successfully treated by direct attack. The vessel concerned was an unnamed anomalous one. It may represent a remnant of the primitive basilar-vertebral anastomosis or of the originally paired basilar artery group (Padget, 1945).[23]

Elkin and Harris (1946)[6] have reviewed arteriovenous aneurysms of the vertebral vessels in the neck, whose diagnosis, they feel, to be the most difficult of all such fistulae.

Diagnosis of these types of vascular anomalies is certainly more accessible with vertebral angiography, as shown by the 2 instances of basilar aneurysm described before. We cannot now agree with Yaskin and Alpers[31] that "The exact diagnosis of an unruptured aneurysm of the vertebral artery during life is no more possible today than it was when Gull stated, nearly eighty-five years ago, that 'Although we may from the circumstances sometimes suspect the presence of aneurysm within the cranium, we have at least no symptoms upon which to ground more than a possible diagnosis.'"

It seems probable that with wider use of vertebral angiography its field of application will become broader. It seemingly would be indicated in those patients in whom air study fails to visualize the posterior part of the third ventricle, the aqueduct of Sylvius and the fourth ventricle. It would be even more useful perhaps in those in whom clinically indicated posterior fossa exploration fails to reveal a cause for the patient's signs and symptoms. This holds especially for those with seizures who have otherwise signs and symptoms of posterior fossa neoplasm and in whom the lesion may well be at the tentorium. Alternatively, it may come to be preferred over air injections as a first diagnostic aid even though (at least in our hands) a general anesthetic is required. Angiography of either carotid or vertebral vessels seems to be readily tolerated in patients with marked increased intracranial pressure and does not carry with it the dangers of disturbing the ventricular equilibrium such as occurs in ventriculography; nor is it necessary to follow angiography with exploration. Whether or not vertebral angiography will permit differential diagnosis of tumor type as well as localization (as is true of many carotid visualizations) remains to be seen. The possible differentiation of meningiomas of the posterior fossa and other cerebellopontine angle tumors by angiography has already been mentioned by Campbell and Whitfield (1948)[2]; certainly it is best to be forewarned of tumor vascularity before planning an operation. Properly timed angiograms could show the chief side of venous outflow from the superior saggittal sinus, of importance in planning a combined supra- and infratentorial attack on cerebellopontine angle and tentorial tumors. Finally, the vexatious differentiation between pontine tumors and encephalitis, demyelinizing disease and primary vascular disease may well be advanced by wider application of this technique.*

SUMMARY

1. A new percutaneous technique for vertebral angiography is described. It has been used in over twenty patients with good visualization in all but two early attempts.

2. The normal vertebral-basilar angiograms are described.

3. Five case reports are given with reproductions of vertebral angiograms showing the type of information which can be obtained. Two of these are cases of basilar aneurysms pictured for the first time ante-

* We wish to thank Dr. Percival Bailey for his guidance and suggestions. Miss Roxanne Pickering, our X-ray technician has been most cooperative with technical details. The photographs are the work of Mr. Willard Huntzinger.

mortem without operation. One shows collateral circulation of the entire cerebrum in a patient with traumatic carotid-cavernous fistula. One concerns a thalamic carcinomatous metastasis, and one describes a patient with posterior fossa arteriosclerosis.

4. The historical development of vertebral angiography is reviewed.

5. A survey is made of the recent publications on aneurysms of the posterior intracranial circulation.

6. The indications and complications of vertebral angiography are discussed.

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VOL. 61, NO. 2

THE DETECTION OF GASTRIC CARCINOMA BY PHOTOFLUOROGRAPHIC METHODS*†

PART I. INTRODUCTION

By JOHN F. ROACH, ROBERT D. SLOAN, *and* RUSSELL H. MORGAN

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A PERUSAL of morbidity and mortality statistics reveals that the incidence of cancer of the digestive system is distressingly high. Approximately 60,000 men and 42,000 women above the age of forty develop gastrointestinal malignancy each year in the United States. Of these, almost 60 per cent die within one year of the time that the diagnosis is made. Moreover, those individuals who do not survive the disease comprise nearly one-half of the deaths resulting from all types of cancer and 5 per cent of the deaths occurring from any cause. Thus it is clear that cancer of the digestive system constitutes one of the serious problems confronting the medical profession today.

Of the various types of neoplastic disease occurring within the alimentary tract, cancer of the stomach is the most prevalent. In men, nearly 40 per cent of the malignant lesions arising in the digestive system are gastric in origin. In women, 30 per cent of such lesions lie within the stomach. The course which gastric cancer pursues is one of relatively short duration. It may be calculated from statistical data recently published by Dorn[1] that the average length of life following the recognition of the disease is of the order of one year and eight months regardless of therapy. It is therefore evident that the methods currently employed in the diagnosis and treatment of cancer of the stomach are, in general, ineffective.

The therapeutic procedures used in the control of gastric cancer have been radiological and surgical. Radiation therapy has been uniformly unsuccessful because of the high resistance that gastric neoplasms exhibit toward any of the radiations which have been available to this time. The record of surgical treatment also has not been satisfactory. Indeed the average five year survival rate of patients having cancer of the stomach lies in the neighborhood of 5 per cent even when optimum surgical methods are employed. The causes of such a low rate have recently been analyzed by Pack[2] who believes that the following four principal factors are responsible: (*a*) the patient is *inoperable* when the diagnosis of the disease is first established; that is, the lesion is so extensive that all operative procedures are precluded; (*b*) the patient is regarded as operable but when the abdomen is opened the lesion is found to be *unresectable;* (*c*) the patient has a resectable lesion but *dies during or shortly after operation;* and (*d*) the patient survives operation but dies from a *recurrence* of the disease or from other causes during the five year period following operation.

At present, Pack has found that approximately 50 per cent of patients who have gastric cancer are inoperable when the disease is first diagnosed. Of the remainder, almost one-half present unresectable lesions. Thus only 25 per cent of persons with gastric malignancy have any change of benefit from surgical intervention. Of these, one-third do not survive operation and of those who do recover[1] over two-thirds die from recurrent disease or from other cause within a few years. Thus the average five year survival rate for patients with gastric cancer reduces to 5 per cent.

The data presented by Pack are admittedly discouraging. A number of statistical

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investigators, however, including Berkson,[3] have found that if a patient with carcinoma of the stomach is resectable and lives for a period of five years following operation, his life expectancy approaches that of individuals free of gastric malignancy. This is graphically illustrated in Figure 1 where the percentage of patients living after gastric resection is plotted as a function of the time following operation (curve B). that even if a patient has a resectable lesion, his chances of avoiding recurrence of the disease and subsequent death under present conditions are only 35 per cent; that is, two-thirds of patients with so-called resectable lesions are beyond surgical cure at the time of operation due to uncontrollable extension of the neoplastic process.

From the findings of Pack and of Berkson it is clear that the poor prognosis and

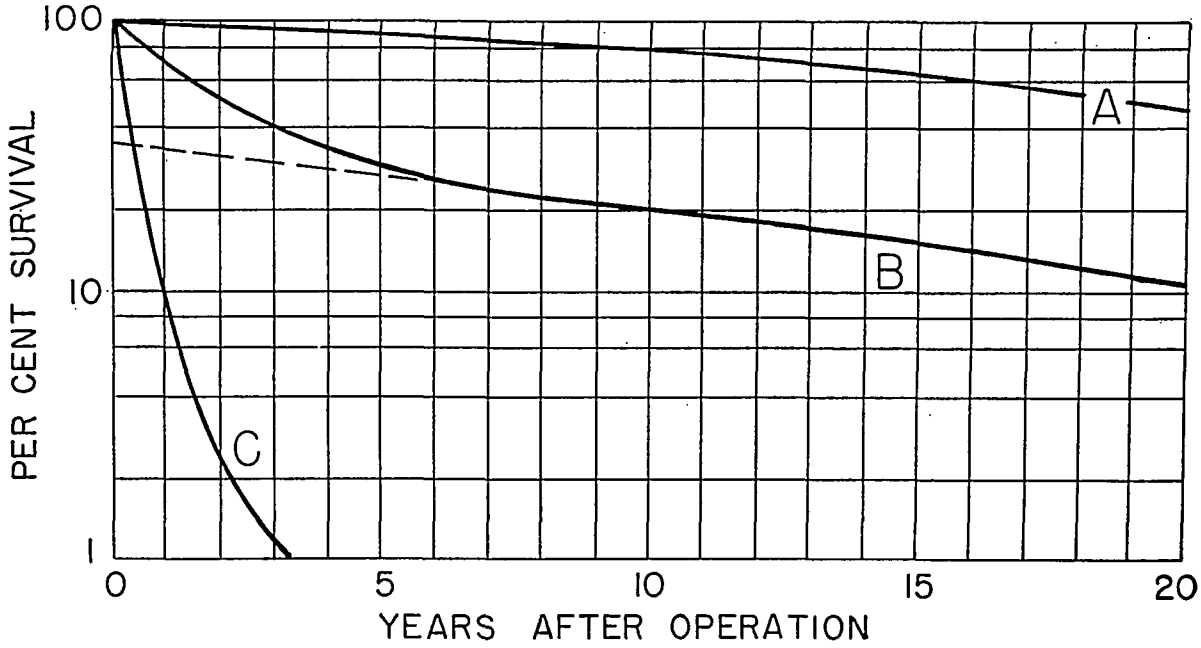


FIG. 1. Survival data for patients with gastric carcinoma. Curve A: normal population; curve B: patients with resectable lesions; curve C: patients with unresectable lesions (after Berkson[3]).

Also included are curves indicating the survival rates of persons in the normal population (curve A) and of persons with unresectable gastric neoplasms (curve C). It will be observed that after five years elapse, the rate of decline of the resection curve is closely similar to that of the normal population curve.

It is evident from the data presented in Figure 1 that surgery has much to offer the patient with gastric cancer. It must be emphasized, however, that the surgical intervention must occur early in the development of the disease process for it will be seen that if the straight-line portion of the resection curve is extrapolated to the left, it intercepts the zero-time axis at a survival value of 35 per cent. This indicates low survival rate of patients with gastric malignancy are due (*a*) to the advanced state of the disease at the time of its diagnosis and (*b*) to the dangers of surgical operation. The latter of these factors can undoubtedly be reduced to insignificance by improvements in preoperative and postoperative care and by advances in surgical and anesthetic techniques. The nullification of the first factor, however, constitutes a more difficult problem and requires that gastric cancer be diagnosed at an appreciably earlier time than is now possible. It has been thought by some that earlier diagnosis might be achieved by a nationwide educational program to inform layman and physician alike of the cancer problem. It is unlikely, however, that such

a program alone will materially affect the cancer death rate. This fact has been strikingly pointed out by Wangensteen[4] who cites the cases of several prominent physicians who were thoroughly conscious of the cancer problem, yet were unable to recognize their own symptoms and subsequently died of carcinoma of the stomach.

Fundamentally, the early diagnosis of gastric malignancy is a problem of finding those asymptomatic individuals in the general population who have the disease. Attention should therefore be directed toward the development of diagnostic procedures whereby large segments of the general population may be examined quickly and easily, at regular intervals, for gastric lesions. At the present time, the roentgenological method probably constitutes the most reliable diagnostic procedure at our disposal for the examination of the stomach and therefore should be explored as a possible means of mass examination. Other procedures such as gastroscopy and gastric aspiration with the study of the gastric contents using the Papanicolaou techniques may be of distinct help, too, but neither of these examinations appears to be of practical value when large numbers of individuals are to be examined. If one also considers the requirement that examinations be repeated at intervals, it is highly improbable that asymptomatic patients will return for either gastroscopy or aspiration. It has been adequately shown in tuberculosis control surveys that the method which attracts the asymptomatic individual is the one which is convenient and without discomfort. Time-consuming or painful procedures will automatically eliminate the greater part of the available voluntary patients. Thus it seems that, for the time being at least, the hope of obtaining early detection of gastric lesions lies in the field of roentgenology.

Conventional roentgen studies of the stomach entail both roentgenoscopy and roentgenography. The first of these two procedures is slow and requires the prolonged services of a highly trained physician. These facts quickly exclude the method as impractical for mass examination of the stomach even before one considers two other inherent objections, namely (*a*) the limited interpretability of present-day fluoroscopic screens and (*b*) the probability of permanent radiation damage to the fluoroscopist. Also, conventional roentgenography of the stomach requires the exposure of films of large size. The use of such films in the examination of large population groups can hardly be regarded as practical, not only because of the initial cost of the films but also because of the expense of time and money in handling, processing and storing the roentgenograms.

Any discussion of the use of roentgen procedures in the early detection of gastric cancer must consider the possible application of photofluorographic methods to the problem. Photofluorography has been extremely successful in the early detection of pulmonary lesions and it therefore may be useful in the discovery of gastric pathology. Furthermore the method is inexpensive and rapid in execution and does not require the services of a fluoroscopist. The principal disadvantages of the procedure include (*a*) the excessively large doses of radiation that until now have been necessary to produce satisfactory photofluorograms of the abdomen and (*b*) its unknown efficiency in the early detection of gastric neoplasms.

The excessive radiation dosage which may occur during photofluorography of the abdomen has recently been overcome by the application of Schmidt optics to photofluorographic camera equipment.[5] With cameras of the Schmidt type, it is now possible to make photofluorograms of the stomach with little more exposure than that used in conventional roentgenography. Thus, the only remaining problem concerning gastric photofluorography is its reliability of diagnosis. In an effort to evaluate this factor, a pilot survey has been established at The Johns Hopkins Hospital in which all patients above the age of forty who are admitted to the Dispensary Out-Patient Clinic of the Hospital during the

course of the study will be examined photofluorographically, for gastric pathology. The equipment employed for these examinations will be described in detail in Part II of this series. It will therefore suffice to say at this time that the apparatus incorporates Schmidt optics, examines patients in the recumbent position and delivers from 0.5 to 2.0 r (including backscatter) per exposure to the patient's skin.

The study has been limited to patients above the age of forty because the incidence of gastric carcinoma in individuals below that age is negligible. The number of nonsignificant cases with which the investigation is burdened will therefore be reduced to a minimum. Even so, statistical data indicate that one may expect to find only one man with gastric malignancy in every 700 men studied; in women, the expected prevalence of the disease is one individual in every 1,200 females. At first glance, it may appear to some that such a yield of pathology will be insufficient to test the photofluorographic method adequately. It is anticipated, however, that within each year of the study between 5,000 and 10,000 patients will be examined and that a minimum of 6 to 12 gastric carcinomas will pass through the unit. Furthermore, although the majority of the patients coming in for examination will have no symptoms referable to the gastrointestinal tract, a few will and these latter cases should increase the incidence of abnormal findings above that which occurs in wholly asymptomatic groups. It is noteworthy in passing that the number of persons whom one may expect to find with carcinoma of the stomach in general population groups of males and females above forty is approximately 1 in 900. Such an incidence may seem small but in reality it is only slightly less than that of significant pulmonary tuberculosis in the general population (1 in 300 to 500). Moreover, even though the yield is small certainly the method will be justified if thereby an early diagnosis of gastric cancer may be accomplished.

It is planned to pursue the survey for a period of approximately five years. During this time, all patients with abnormal photofluorograms will be restudied with conventional roentgenoscopic and roentgenographic techniques. Those who present changes suggesting gastric carcinoma thereupon will be operated upon surgically. As the study proceeds, survival data of operated patients whose diagnoses are confirmed pathologically will accrue and a comparison of such data with those presented in curve B of Figure 1 will permit an evaluation of the efficacy of the photofluorographic process in reducing the gastric cancer mortality.

As a part of the investigation it is also planned to collect a group of approximately 1,000 asymptomatic individuals and to examine them photofluorographically for gastric pathology at intervals of six months over a five year period. From this study it is hoped that an estimate of the interval at which photofluorographic examinations of the stomach should be repeated in the general population may be determined.

In subsequent publications of this series, the results of the investigation will be reported. It must be stated at this time that no preconceived notions regarding the place of photofluorography in the cancer problem are held. The study has been undertaken to determine the reliability of the photofluorographic process in the early detection of gastric malignancy, a process that has been virtually untried until the present time. The next paper of this series will describe in detail the photofluorographic equipment used in the investigation.

SUMMARY

It has been statistically shown that cancer of the stomach is a prevalent and rapidly fatal disease for which the only promising form of therapy, available today, is surgery. If surgery is to be successful resection must be done early in the course of the disease, prior to the appearance of symptoms. Thus, methods must be developed whereby large segments of the

population may be examined at regular intervals to find the asymptomatic but positive case. The most feasible method for carrying out this sort of an examination is the photofluorographic process. A pilot study has been established to determine the efficiency of this method using the male out-patient population of this hospital above the age of forty. The study will be pursued for a period of five years. Subsequent papers of this series will report the experimental findings.

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THE DETECTION OF GASTRIC CARCINOMA BY PHOTOFLUOROGRAPHIC METHODS*†

PART II. EQUIPMENT DESIGN

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I. INTRODUCTION

THE success with which the photofluorographic process has been employed in the examination of large population groups for the early detection of chest pathology has led many radiologists to consider its application to the mass study of carcinoma of the stomach. By means of small film techniques it should be possible to examine rapidly and inexpensively large segments of the nation's adult population for the disease at regular intervals. Furthermore, the use of small film methods should reduce the time expended by physicians in the procedure to levels far below those needed in other roentgenologic techniques such as fluoroscopy and large film roentgenography; photofluorography therefore should effectively overcome the obvious impracticability that has been cited in the use of these latter procedures in mass roentgenologic studies of the stomach.

In spite of the ease with which photofluorography may be used in the study of gastric cancer, many radiologists have advised against such an application. It has been pointed out that although there is general agreement among the medical profession that roentgenologic methods are extremely useful in the early detection of pulmonary tuberculosis, there are no reliable data which indicate that these methods will be equally valuable in the early detection of carcinoma of the stomach. Furthermore, in the past, a combination of fluoroscopy and roentgenography has always been used in the examination of the stomach for pathology of any kind; the use of film techniques alone is completely untried. Some skepticism regarding their usefulness therefore seems justified. In addition to these objections, it is also known that for an adequate examination of the stomach by photofluorographic methods, undesirably large doses of radiation must be employed because of the relative inefficiency of the photofluorographic process. Almost *twenty* times as much radiation is needed in a photofluorographic exposure using equipment generally available today as in the making of a conventional roentgenographic film. Since conventional roentgenography of the stomach requires an exposure of the order of 0.5 roentgen, including backscatter, at the skin surface for every film made, it will therefore be evident that if a series of six films is exposed for each patient studied by the photofluorographic method (the number possibly required for a satisfactory examination) a total of 60 roentgens will be delivered to the patient's skin. Such an exposure, even though it may be divided among several fields, is certainly not inconsiderable especially when it is remembered that if pathology is suspected, conventional roentgenologic procedures will be necessary to confirm the impression and therefore require additional exposure.

The relatively large doses of radiation needed in the performance of gastric photofluorography have been a serious impediment to the application of the procedure on a mass basis. Recently, however, the employment of Schmidt optics in photofluorographic camera equipment and the development of faster fluorescent screens have made it possible to increase the efficiency of the photofluorographic process by a factor of almost twelve. By

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† The work described in this paper was done under a contract between the National Cancer Institute and The Johns Hopkins University.

taking advantage of these contributions, photofluorography can now be performed with the expenditure of little more energy than that used in conventional roentgenography and, from a technical standpoint, gastric photofluorography has become an entirely practical procedure so long as these newer developments are used. Of course, the argument still prevails that gastric photofluorography is an untried procedure and that its usefulness in the early detection of carcinoma of the stomach may be doubted. However, since the method may be made free of technical difficulties and since the early detection of gastric cancer by all other methods is either unreliable or involves procedures that are generally impractical, it has been thought wise to establish a photofluorographic installation by which large numbers of persons within the age group in which carcinoma of the stomach is especially prevalent may be studied. Possibly from such an investigation a technique may be developed that will prove as valuable as photofluorography of the chest in the detection of pulmonary tuberculosis.

The remainder of this paper will be devoted to a description of the technical facilities which have been established for the study. Before we proceed to these discussions, however, it must be emphasized that no preconceived notions are held regarding the place that gastric photofluorography may have in the future in the diagnosis of carcinoma of the stomach. The investigation is being pursued only to determine whether or not the method, untried until the present and now relatively safe to perform, will have value.

II. TECHNICAL EQUIPMENT

The photofluorographic installation which has been established for the investigation of mass roentgenographic methods in the diagnosis of gastric carcinoma differs considerably from the small film units currently used in mass roentgenography of the chest. The nucleus of the installation is a 70 mm. Schmidt camera, constructed by the Danish engineer, Helm, and recently brought to this country by the Tuberculosis Control Division of the United States Public Health Service.[2] This camera has an f/ number rating of 0.75 and has a speed approximately 5 times greater than that of photofluorographic cameras commonly in use. Furthermore, measurements of resolving power made at the National Bureau of Standards indicate that the ability of the camera to record detail is equal to that of conventional cameras using 70 mm. film, in spite of its speed.

The high speed of the Schmidt camera is achieved by virtue of its unusual optical system in which the principal lenticular element consists of a large spherical mirror which picks up the light from the fluorescent screen and reflects it directly on the photofluorographic film. Since the aperture of the mirror is much larger than that which can be attained in lenses of the conventional refractor type, the proportion of the light delivered to the film from the screen in the Schmidt system is greater than in ordinary lenses.

A schematic diagram of a Schmidt camera is shown in Figure 1. There it will be seen that light emitted from a fluorescent screen *S*, is reflected by the spherical mirror *M*, on the photofluorographic film *F*, which itself is curved into a semispherical configuration. In addition to the spherical mirror, a single element, aspherical lens *L*, is placed in the optical system between the screen and mirror to correct for aberrations introduced by the mirror. An interesting constructional detail of this lens system is the positioning of the film between the fluorescent screen and the principal lenticular element, the mirror. Also, since the film must face the mirror it faces away from the fluorescent screen; its rear surface must therefore be protected from light emitted directly from the screen. This protection is accomplished by the enclosure *C*.

The Schmidt camera manufactured by Helm is approximately 18 inches in length; its diameter is about 13 inches. The camera

uses 70 mm. perforated film and produces an image 55 mm. square. A manual type film advance mechanism is used and includes an electrical interlock system which prevents the making of an exposure until the film has been advanced following the previous exposure. The focusing of the camera is unusually simple. An opening in the center of the mirror permits one to observe the surface of the film from the rear of the camera and thereby to focus the instrument under visual control. Interestingly, in the focusing process it is the film carriage that is moved rather than the lenticular elements.

The fluorescent screen employed in the installation is a Patterson type E-2, a screen which has approximately twice the sensitivity of the recently obsolete type B screen. With the increased speed provided by the Schmidt camera, this screen makes it possible to take photofluorographic films of the abdomen with exposures ranging from 50 to 100 milliampere-seconds at a tube potential of 95 kv. (peak) and at a tube-screen distance of 36 inches. This corresponds to a roentgen dosage at the skin surface of approximately 0.5 to 2 r including backscatter, or only slightly more than the dosage delivered in conventional roentgenography.

The size of the field covered by the photofluorographic screen is 15 inches square. Since the image size of the film is 55 mm. square, the minification of the camera is therefore seven times. Such a minification is not so great that the mucosal patterns of the stomach and small intestine cannot be clearly seen in the film.

In addition to the camera and screen, the photofluorographic system includes a special Liebel-Flarsheim cross-hatched stationary grid placed in apposition to the rear surface of the screen to prevent scattered radiation from fogging the fluorescent images. Since the quantity of scattered radiation to be removed during abdominal filming is materially greater than that during roentgenography of the chest, the conventional wafer grid used in chest photofluorographic units did not prove adequate in this installation.

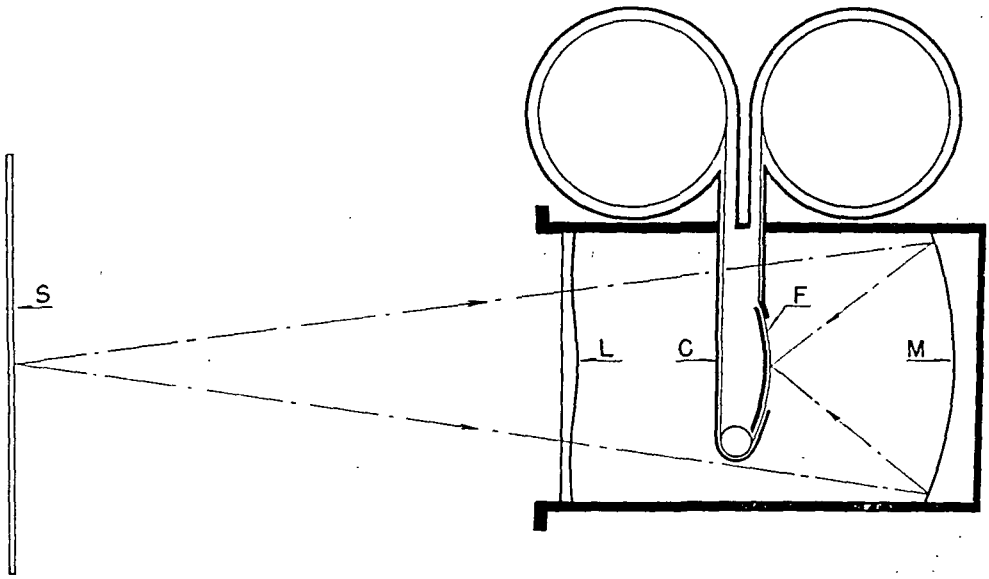


FIG. 1. Schematic diagram of Schmidt camera. *M*, spherical mirror; *L*, aspherical lens; *F*, photofluorographic film; *C*, film enclosure; *S*, fluorescent screen.

Early in the design of the photofluorographic installation, it was decided to arrange the equipment so that the examination of the patients might be carried out only in the recumbent position. It was realized that if the patients were examined in the erect posture, large regions of the stomach in and near the fundus would not be satisfactorily visualized in mucosal relief or gross outline; certainly, it was

desired that such incompleteness of examination should be avoided if at all possible. It was therefore decided to mount the grid, fluorescent screen and the photofluorographic camera below a conventional horizontal roentgenographic table. Such an arrangement, however, introduced immediate difficulties. As stated heretofore, the Helm camera is 18 inches long; furthermore, the screen-camera distance that is required approaches 42 inches. Thus if conventional mounting of screen and camera were followed and the end of the camera allowed to rest on the floor below, the surface of the table would occupy a position 5 feet above the floor. Such a position is obviously inconveniently high. The possibility of hanging the grid-screen-camera assembly above the table with the roentgen tube located under the table was then considered. However, it was immediately recognized that such an arrangement would be dangerous in that the grid-screen-camera assembly might break loose from its mounting and crash on the patient below. Finally the arrangement illustrated schematically in Figure 2 was investigated and found to overcome satisfactorily the foregoing difficulties. In this arrangement, the grid *G*, and fluorescent screen *S*, of the photofluorographic system are mounted in a light-proof hood *H*, directly below the surface of the roentgenographic table *R*. The light from the screen is directed downward and falls on a front-surfaced Pancro mirror *M*, whose surface is placed at 45° to the plane of the screen. This mirror redirects the fluorescent light into the Schmidt camera *K*, whose long axis now is parallel to the long axis of the roentgenographic table. With this system the arrangement of the various components below the roentgenographic table is such that the table top may be at a convenient level above the floor and the end of the camera may be in a satisfactory position for the loading and advancing of the film. It may be argued by some that the loss of light incurred by the mirror is a serious disadvantage to the system. However the loss is less than 7 per cent and is therefore of no concern.

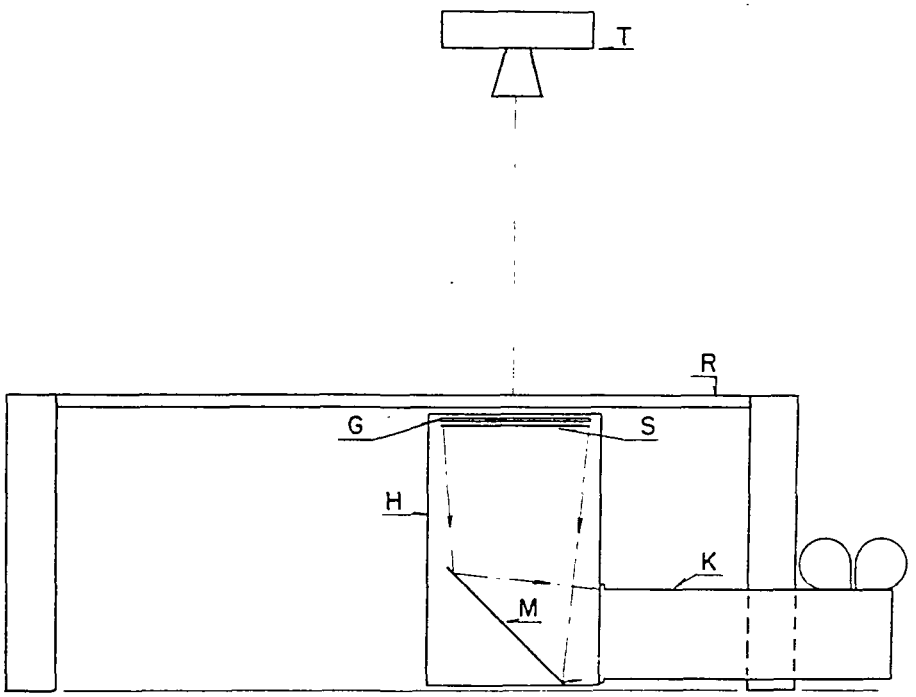


Fig. 2. Schematic diagram of photofluorographic unit developed for mass roentgenography of the stomach. *T*, roentgen tube; *R*, roentgenographic table; *G*, wafer grid; *S*, fluorescent screen; *H*, light-proof hood; *M*, front-surfaced mirror; *K*, Schmidt camera.

It was necessary to choose the position of the 45° mirror rather carefully in the installation. Early experiments indicated that if the mirror were placed too close to the fluorescent screen, light from the screen could reflect back to the screen surface and badly fog the fluorescent images appearing on it. These reflection problems, however, were found to be effectively corrected by increasing the distance between the screen and mirror to the point at which light from the screen could not be reflected back to the screen under any circumstances. The position of the mirror shown in Figure 2 fulfills this requirement.

The photofluorograph is powered by a standard 200 milliampere, four-valve generator operating at 95 kv. (peak) and controlled by a photoelectric automatic timer of essentially conventional design.[3] The phototube scans a small area near the center of the field of examination. Exposure times are of the order of 0.5 second. A rotating anode tube with a focal spot 1.5 mm. square is employed and the tube-screen distance is 36 inches. A photograph of the complete installation is shown in Figure 3.

An impression of the quality of the films obtained with the unit may be gained from Figure 4 where films taken in the anteroposterior and right anterior oblique position after the ingestion of a small amount of barium and in the posteroanterior and right anterior oblique position after the ingestion of a large amount of barium are reproduced. These positions permit one to view the mucosal pattern and gross outline of the major portions of the stomach. It remains to be seen how well pathologic processes within the stomach may be detected by the method.

It is planned to examine 40 patients per day during the next several months as a

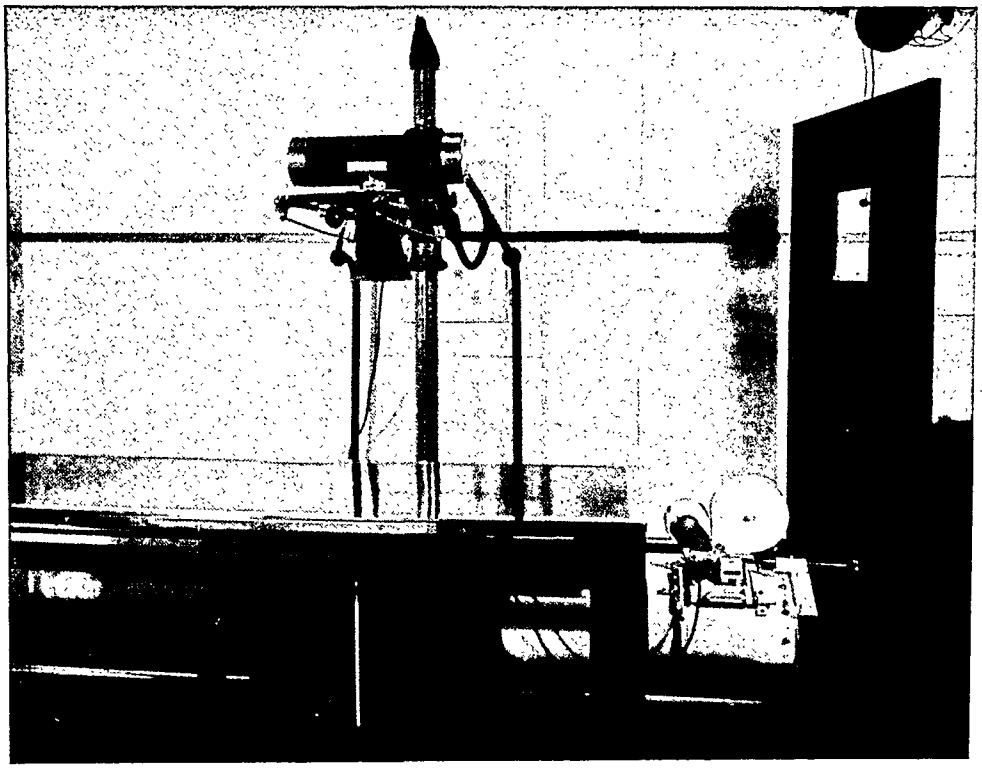


FIG. 3. Photograph of photofluorographic unit developed for mass roentgenography of the stomach.

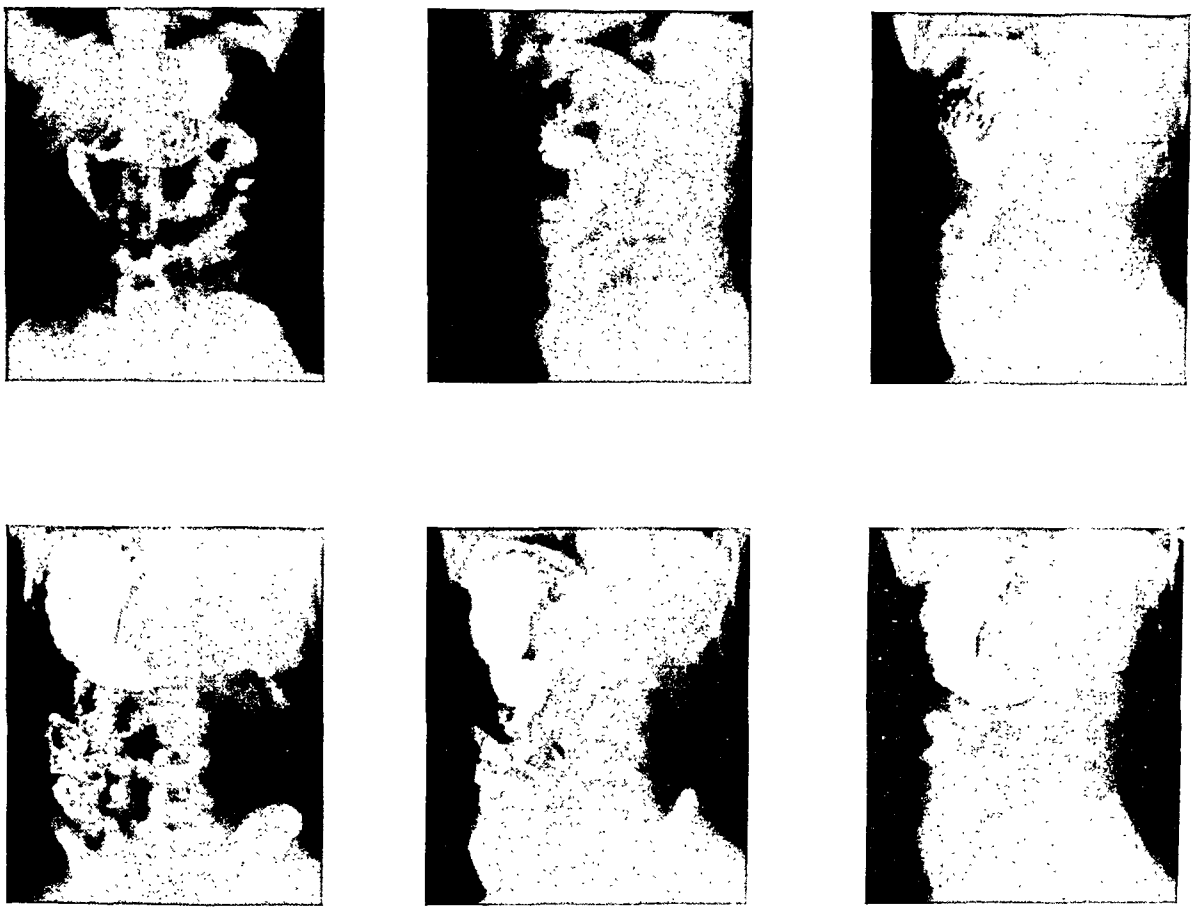


FIG. 4. Reproductions of 70 mm. photofluorographic films of the stomach taken with the patient in the recumbent position. The upper three films were made after the ingestion of 1½ ounces of barium mixture; the lower three films were made after 5 ounces of barium had been ingested. In each case two views in the right anterior oblique projections were taken to demonstrate the progression of peristalsis.

pilot study to determine the best technical procedures to be followed with the equipment. The results of this investigation will be reported in subsequent publications. If the data are encouraging, much more extensive studies on large population groups with the performance of possibly 200 examinations per day will be undertaken. Preliminary trials indicate that the equipment should be able to accommodate such a volume of work within an eight hour day if not more than six films per patient are made.

III. SUMMARY

Photofluorographic equipment by which the roentgenographic examination of large population groups for gastric carcinoma may be carried out with the application of little more radiation than that employed in conventional roentgenography is described. The apparatus consists of a standard 200 milliampere generator, a rotating anode tube, and a grid-screen-camera assembly using a Patterson type E-2 screen and a Schmidt camera. The grid-screen-camera assembly is mounted beneath a horizontal roentgenographic table to permit the examination of patients in the recumbent position, thereby assuring a completeness of study not attainable with other positions. Results of the use of the equipment in the early detection of gastric carcinoma will be reported in subsequent papers.

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VOL. 61, NO. 2

THE AZYGOS LOBE: ITS INVOLVEMENT IN PULMONARY DISEASE*†

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A COMMON anomaly found in reading roentgenograms of the chest is the presence of an azygos lobe or fissure. This occurs so frequently that no special report would be of interest if it dealt with this condition in the otherwise normal chest. I wish, however, to report a series of cases in which this anomaly was involved in various pulmonary diseases. Localization of pulmonary pathology in this area is sufficiently unusual to be worthy of note.

In the normal human being the azygos vein travels cephalad in the posterior portion of the right half of the thorax, lying anterior to the inner surfaces of the ribs and posterior to the parietal pleura. It usually ascends to about the fifth rib and then curves anteriorly to join the superior vena cava just before this structure enters the right auricle. The exact point of entry varies somewhat, but in the normal individual the azygos vein is medial to the right upper pulmonary lobe and to the parietal and visceral pleurae as it crosses the root of the lung. In the condition diagnosed as azygos lobe the vein runs lateral to its normal position. When it curves forward and medially, therefore, to join the superior vena cava it encounters the right upper lobe and in traversing it creates a new fissure in the lung. It does so by invaginating the posterior parietal pleura, and creates a cleft in the visceral pleura and in the right upper lobe. A frontal section through the right lung at this point (Fig. 1) would reveal the structures to be in the following order, going medially—right upper lobe, visceral pleura, parietal pleura, azygos vein, parietal pleura, visceral pleura, azygos lobe, visceral pleura, parietal pleura, mediastinal structures. The vein itself is never intrapleural.

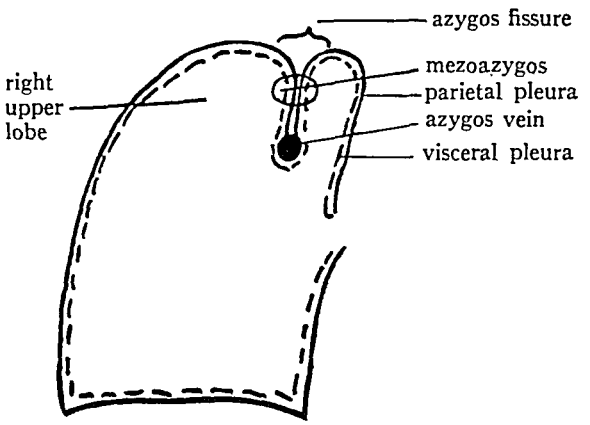


FIG. 1. Diagram of frontal section of the chest when azygos lobe is present, illustrating the anatomical relationships.

As a result of this anomaly, a septum is formed which is composed of two layers of the parietal pleura. This is thus a defect of septation rather than of lobation. This septum is known as the mesoazygos from its analogy with the mesentery. The azygos vein traverses its free edge in an analogous fashion to the bowel. Because of this septum of parietal pleura the azygos fissure differs from all the other pulmonary fissures. It is the only one which persists in the pleural space after the lung has been removed.

Occasionally disease processes affecting the right upper lung field will involve the azygos lobe alone, or its fissure, or the remainder of the right upper lobe without affecting the extra lobe. Pneumothorax will separate the right upper lobe from the

* From the Tuberculosis Service, Dr. Gerald D. Guilbert, Chief.

† Published with permission of the Chief Medical Director, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.



FIG. 2. Case I. Azygos lobe in an otherwise normal chest.

azygos lobe just as it does the upper middle and lower lobes. Pleural effusion may similarly separate the lobes, creating an azygos interlobar effusion. Consolidation may affect the anomalous lobe alone or the remainder of the upper lobe, sparing the azygos.

CASE I is that of a tuberculous effusion in a patient with an azygos lobe. Figure 2 shows the chest before the onset of the effusion and illustrates the appearance of an azygos fissure in an otherwise normal chest. Figure 3 shows a general pleural effusion with azygos interlobar effusion. Figure 4 pictures the condition after resolution of the effusion, leaving a chronic fibrous pleurisy of the general pleural space and the azygos interlobar fissure.



FIG. 4. Case I. Chronic fibrous interlobar pleurisy.

CASE II is that of a patient with bilateral pulmonary tuberculosis. Figure 5 illustrates the



FIG. 3. Case I. Azygos interlobar effusion with general pleural effusion.

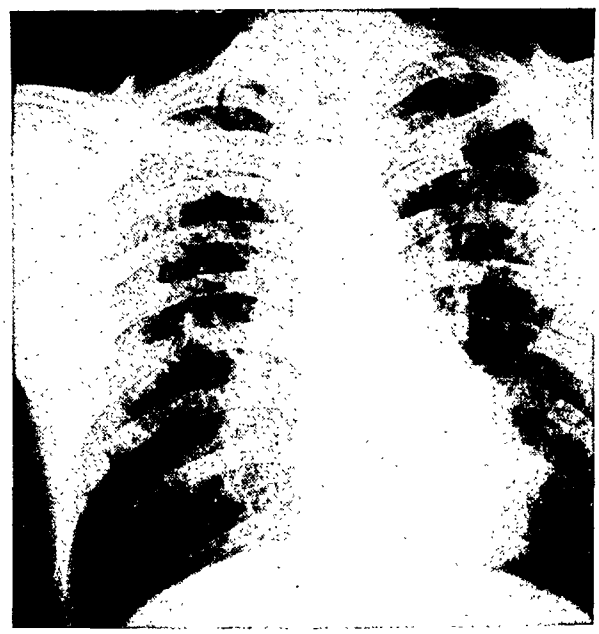


FIG. 5. Case II. Far advanced tuberculosis in a patient with azygos lobe.



Fig. 6. Case II. Artificial pneumothorax has been induced and the azygos lobe can be seen clearly separated from the right upper lobe.

condition, showing the azygos fissure, with little or no involvement of the azygos lobe in the disease process. In Figure 6 artificial pneumothorax has been instituted on the right. The azygos lobe appears well expanded and well aerated and clearly separated from the remainder of the right lung. The disease area is

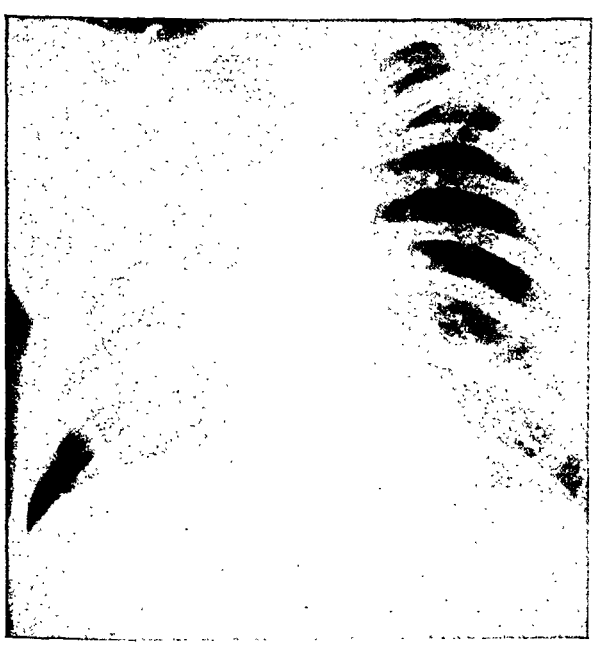


Fig. 7. Case III. Blastomycosis affecting the entire right upper lobe but leaving the azygos lobe as a clear oval area of increased radiolucency.



Fig. 8. Case IV. Pulmonary tuberculosis affecting the azygos lobe without the right upper lobe being involved.

held out by adhesions. The azygos lobe appears to be widely adherent to the mediastinum. However, subsequent roentgenograms revealed that the azygos lobe collapsed and disappeared from sight. It was not visualized at a subsequent intrapleural pneumonolysis. However, on



Fig. 9. Case IV. Same case with an overexposed film revealing the presence of multiple cavities.

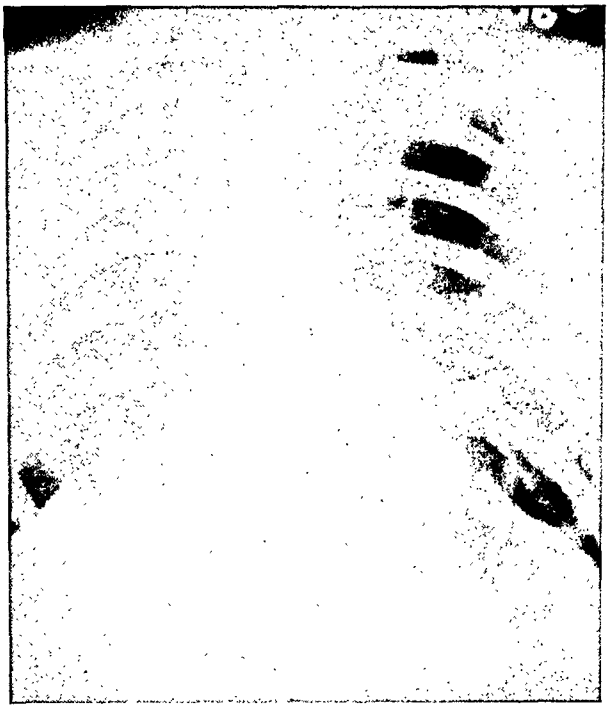


FIG. 10. Case v. Far advanced tuberculosis involving the major portion of the right lung.

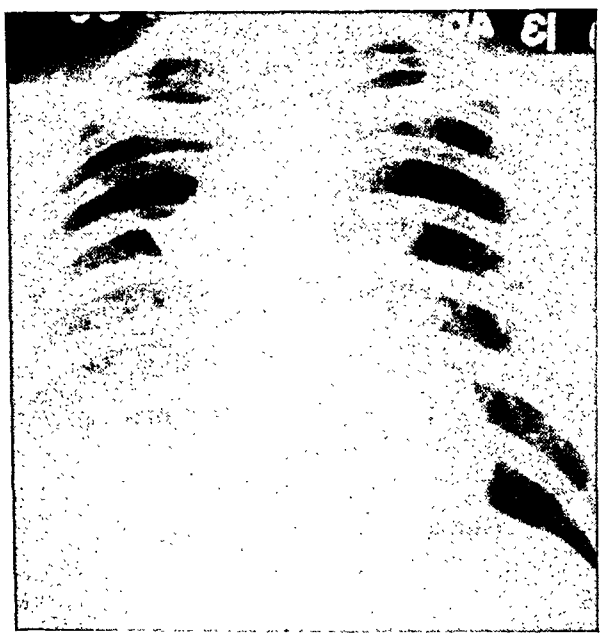


FIG. 11. Case v. Artificial pneumothorax has been induced. The right upper lobe has become entirely atelectatic.

later roentgenograms, a linear shadow could be seen in the region of the previously seen azygos fissure; this probably represented the reduplication of the parietal pleura as seen in Figure 1.

CASE III is one of pulmonary blastomycosis*

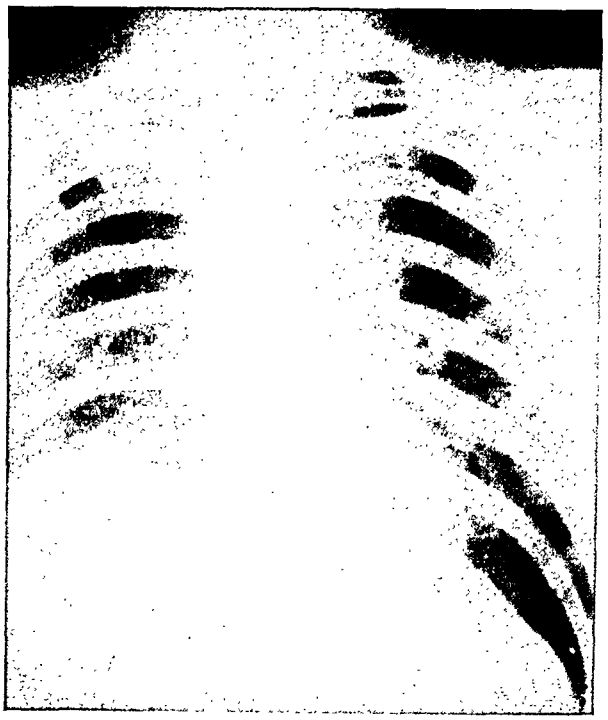


FIG. 12. Case v. "Peudo-azygos" lobe due to atelectasis and fibrosis of the right lung after the pneumothorax was abandoned.

in which the entire right upper lobe was involved, sparing the azygos lobe (Fig. 7).

CASE IV is a patient with pulmonary tuberculosis affecting the azygos lobe alone (Fig. 8 and 9†).

CASE V illustrates a "pseudo-azygos" lobe developing in the right upper lobe which was affected by extensive tuberculosis and was treated with artificial pneumothorax. Atelectasis developed while the lung was collapsed and the shrunken upper lobe now resembles an azygos lobe (Fig. 10, 11 and 12).

SUMMARY AND CONCLUSIONS

The azygos lobe and fissure may be involved by pulmonary and pleural disease processes similar to the other lobes. Illustrative cases are presented. A knowledge of the roentgen appearances of these changes may be of value in the interpretation of an occasional atypical roentgenogram.

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* Permission to use this case was kindly granted by Dr. M. Lustok, Consultant on Chest Diseases; it will reported in greater detail individually.

† Permission to use these roentgenograms was kindly granted by Dr. J. Marks, Roentgenologist at Milwaukee County General Hospital.

Vol. 61, No. 2

OCCURRENCE AND DIAGNOSIS OF DILATATION OF THE AORTA DISTAL TO THE AREA OF COARCTATION*

By FELIX G. FLEISCHNER, M.D.
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THERE is little concerning coarctation of the aorta of the adult type that is not generally known. The anatomical changes are fully recognized. The clinical picture, including diagnosis, prognosis and complications, has been analyzed.[1,2,3] The surgical treatment has added some new details to our knowledge and has improved the prognosis.[4,5] Angiocardiography has brought to light an "atypical type of coarctation of the aorta, with absence of the left radial pulse."[6]

The diagnosis is based upon a strong pulse in the upper extremities, combined with a weak or absent pulse in the lower extremities, and confirmed by the evidence of collateral circulation and by the roentgen signs.[7,8] These roentgenologic signs, particularly the notching of the ribs, have special significance in that sometimes they are observed incidentally, and first call attention to the presence of this cardiovascular anomaly.

It has been known from postmortem findings that the aorta is often dilated in a bulbous fashion just beyond the site of the coarctation. This dilatation may be due to congenital weakness of the wall of the aorta or to eddy formation beyond the constriction or to both. Gross, recently reporting to this Association on surgical management of coarctation of the aorta, stated that this dilatation of the aorta may cause difficulties. The proximal and distal aortic stumps have to be anastomosed and this may be difficult if they are greatly different in caliber; moreover, the thinning of the wall may complicate the suturing. Prior knowledge of such dilatation may even influence the indication for this operation.

This statement by Gross has prompted me to report on the following observation:

A male patient, aged thirty-three, was seen at the Beth Israel Hospital in July, 1943. He presented the complete catalogue of the classical signs and symptoms of coarctation of the aorta, including also the roentgen signs.

In roentgenoscopy after swallowing barium the patient showed an unusual bending of the esophagus to the right and anteriorly (Fig. 1). According to the topographic relation between esophagus and descending aorta, this finding suggested the presence of a spindle-shaped dilatation of this portion of the aorta.

The patient died of a cerebral hemorrhage caused by rupture of an aneurysm of the right middle cerebral artery. The autopsy report stated: "In the distal portion of the aortic arch, 0.3 cm. distal to the physiologic scar of the ductus arteriosus, a narrowing of the aortic lumen was found. Seen from above, the aorta forms a tunnel leading into a slit-like lumen of 0.15 cm. in diameter. Distal to the coarctation the aorta is dome shaped. A probe can be passed through the narrowing. . . . The aorta measures 30 mm. in diameter above the stricture, 45 mm. below."

Before opening the chest, Dr. M. J. Schlesinger, pathologist, made an injection preparation with lead phosphate. A roentgenogram, taken in the left oblique position to match the clinical film, is shown here (Fig. 2). Clearly visible are the filled left ventricle, its thickened wall, the dilated ascending aorta, the dilated great vessels with the wide collateral pathways, the constriction of the descending aorta and the spindle-shaped dilatation distal to it. From the comparison of the antemortem and postmortem films it is evident that the displacement of the esophagus was caused by the dilatation of the aorta. Correctly interpreted, it is diagnostic of such a dilatation. This observation has been made in 2 other instances.

* From the Department of Radiology, Beth Israel Hospital and Harvard Medical School. Presented at the meeting of the New England Heart Association, March 29, 1948.

Discussion of the differential diagnostic significance of this displacement of the esophagus is not intended. Dilatation and tortuosity of the descending aorta not infrequently cause a similar displacement of the esophagus and a primary or metastatic growth in the mediastinum as well as a prevertebral abscess may occasionally produce similar pictures. This observation is presented solely to call attention to the roentgenologic recognition of this anatomic feature in instances of established coarctation of the aorta.



FIG. 1. Clinical roentgenogram, left oblique view. The barium-filled esophagus curves to the right anteriorly, starting this deflection just above the level of the carina.

SUMMARY

In coarctation of the aorta there may occur a bulbous or spindle-shaped dilatation of the descending aorta immediately beyond the constriction. This dilatation can be recognized reoentgenologically by a typical displacement of the esophagus. In cases where operation is planned, knowledge of this anatomical detail is of value to the surgeon.

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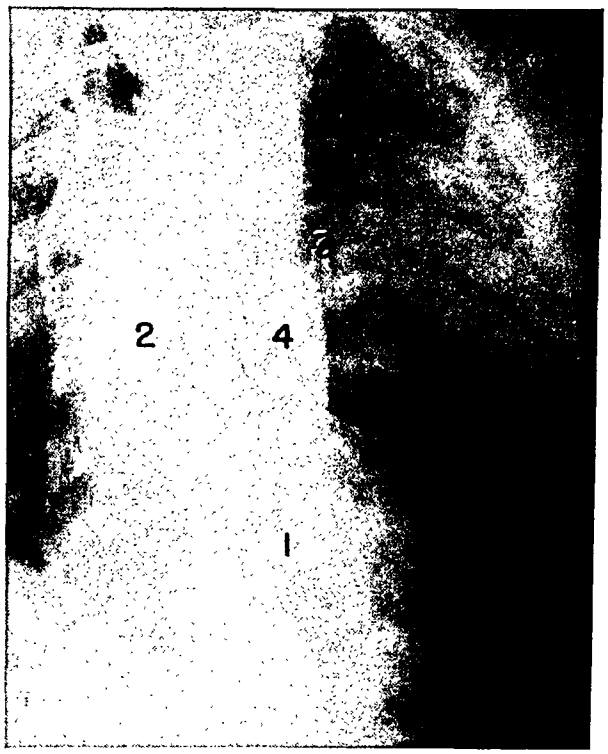


FIG. 2. Postmortem roentgenogram, after opacification of heart and vessels, left oblique view. Retouched. The left ventricle (*1*), ascending aorta (*2*) and the stricture at the junction (*3*) of the aortic arch and the descending aorta are visible. The bulbous dilatation of the descending aorta (*4*) corresponds, in location and shape, to the displacement of the esophagus on the clinical roentgenogram.

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LEFT ATRIAL CALCIFICATION IN RHEUMATIC HEART DISEASE*

By BERNARD S. EPSTEIN, M.D.
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THE roentgenologic visualization of the walls of the left atrium by endocardial calcification arouses interest not only because of its rarity but also on account of the information made available concerning anatomical relationships. Begg[1] recently reported a patient with extensive calcification of the left atrium and another is mentioned by Kerley.[11] Together with the 3 reported here, there are but 5 such patients in the available literature in which the diagnosis was made roentgenologically during life. Recently Frade Fernandez and Torres Ruiz[4] reported an instance of total calcification of the left atrium following an old mural endocarditis, but the condition was unrecognized roentgenologically. Stewart and Branch[13] reported with pathologic observations a similar case in 1924, and noted the rheumatic etiology.

Left atrial calcification may occur following retrogressive myocardial or endocardial damage. The underlying damage in the present cases in all probability was the endocardial lesion originally described by MacCallum.[9,10] This occurs characteristically as a thickened, corrugated plaque on the wall of the left atrium extending upward from the root of the posterior leaflet of the mitral valve. While the MacCallum plaque is a frequent consequence of rheumatic endocarditis, calcification within the plaque is relatively uncommon. Gross[6] could find but one instance in the 87 cases studied histopathologically. The description of the microscopic changes by Gross,[6] Von Glahn[15] and Von Glahn and Pappenheimer[16] deserves careful study.

Calcification of the left atrium has also been described as part of the syndrome of metastatic calcinosis. This is a rare condition, and to my knowledge there is no reported instance in which the diagnosis was made roentgenologically during life. This type of calcification occurs without previous endocardial damage, and in the 2 cases observed by me and previously reported by Grayzel and Lederer[5] was of a delicate, egg-shell consistency which was difficult to identify on the postmortem roentgenograms of the heart.

The present communication is concerned with 3 patients with rheumatic heart disease and mitral stenosis and insufficiency in whom the left atrial calcification was identified and studied during life.

CASE REPORTS

CASE 1. A. W. (Hosp. No. 296699), female, aged forty-five, was first aware of her cardiac condition after an episode of dyspnea on exertion at the age of twenty-five. There was no history of rheumatic fever. Physical examination at the age of thirty-two revealed a loud apical presystolic murmur ending in a sharp first sound. The second pulmonic sound was accentuated, and her blood pressure was 120/80. Teleroentgenographic examination of the chest at that time showed no change in the heart outline, and electrocardiographic examination was normal.

Roentgenologic examination of the chest three years later showed a prominence of the upper left heart border interpreted as a "mitral contour." Her physical signs were unchanged. Auricular fibrillation appeared at that time.

One year ago she was admitted with bronchopneumonia and physical examination revealed a loud apical systolic and diastolic murmur, auricular fibrillation and bronchopneumonia.

Fluoroscopic and roentgenographic examination of the chest showed the heart to be triangular in appearance. The entire left atrium was outlined by calcification, and large deposits were also present in the mitral leaflets which were depressed to about 1.5 cm. above the middle third of the left diaphragm. The left atrial wall was within the heart contour, and its right border approached the right heart border

* From the Radiologic Service of M. G. Wasch, M.D., The Jewish Hospital of Brooklyn, Brooklyn, N. Y.

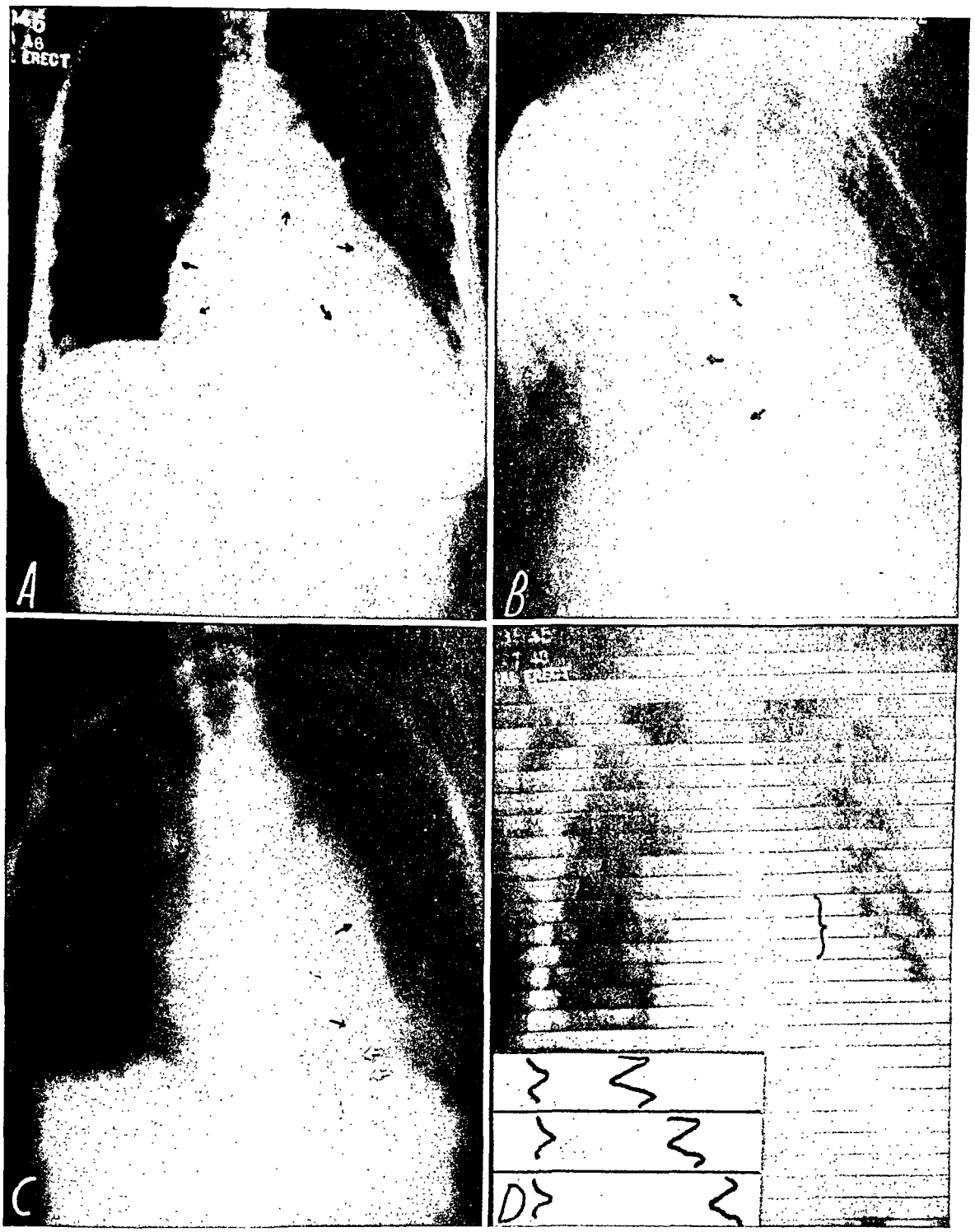


FIG. 1. Case 1, *A*, overexposed teleroentgenogram. The periphery of the left atrium is outlined by the calcified endocardium (black arrows). Calcification of the mitral valve is present (white arrows). *B*, right anterior oblique roentgenogram. The black arrows indicate the posterior wall of the left atrium. Only the segment in close apposition with the esophagus lies within the displaced esophageal arc. Above and beneath, the calcified left atrial wall is appreciably separated from the esophagus, indicating that the posterior displacement of the esophagus does not accurately portray the posterior wall of the atrium. *C*, laminagram taken 12 cm. from the posterior chest wall. The black arrows indicate the atrial calcifications, and the white arrows the mitral valve calcification. *D*, kymogram. The insert shows the pulsation of the atrial wall in relation to the ventricular pulsation. During atrial systole the ventricle is in diastole.

closer than the left side approached the left heart border. The left main bronchus was not elevated, and a space of 1.5 cm. existed between the superior wall of the left atrium and the inferior margin of the left main bronchus. In the right anterior oblique position there was close approximation of the point of greatest convexity of the calcified posterior wall of the left atrium to the esophagus, but above and beneath this site the atrial contour curved away from the esophagus. The thickness of the calcific shadow was 2 mm. in its greatest depth.

Laminagraphic examination of the chest showed the mitral valve calcifications to better advantage, and the left atrial calcification was somewhat more clearly portrayed.

Kymographic examination showed opposing pulsations of the right ventricle and left atrial calcifications, definitely localizing the deposits to the walls of the atrium. The height of the ventricular waves was 0.7 cm. and of the atrial wave 0.3 cm.

CASE II. A. O'S. (Hosp. No. 218646), female, aged thirty-five, had chorea at the age of nine. When seen during an episode of bronchopneumonia at the age of nineteen she had a loud blowing apical systolic murmur and a pericardial friction rub. Teleroentgenographic examination of the chest at that time revealed prominence of the middle of the left heart border in addition to the bronchopneumonic changes. Electrocardiographic examination showed erect, high, notched P waves in the first and second leads.

At the age of twenty-three she had an episode of congestive heart failure with dyspnea, orthopnea, palpitation, vomiting, weakness and cough. Physical examination disclosed a loud apical systolic and diastolic murmur and a diastolic thrill at the apex. Auricular fibrillation appeared at this time. Since then she has been observed during several bouts of congestive failure, and her response to treatment has been excellent.

Fluoroscopic and roentgenographic examination of her heart revealed a triangular configuration when she was twenty-eight and thirty-three years old, and no change occurred over this five year period. There was considerable enlargement of the right ventricle and less left ventricular enlargement. The left atrium displaced the esophagus posteriorly and to the right. A calcific deposit was seen in the midportion of the left border of the left atrium about 0.5 cm. from the heart border. At first this was thought to be a pericardial plaque, but fluoroscopic and kymographic studies revealed that during ventricular systole the calcification assumed a position corresponding to atrial diastole. The amplitude of pulsation of the ventricle was 1.2 cm. and of the atrial calcification 0.3 cm. The left main bronchus was not elevated and was separated from the left atrial calcification by 0.8 cm. A considerable portion of the right lateral border of the heart was formed by the dilated left atrium.

CASE III. R. S. (Hosp. No. 252624), female, aged forty-nine, had rheumatic fever at the age of twenty years. Physical examination during her fourth pregnancy at the age of twenty-nine disclosed systolic and presystolic apical murmurs, a systolic apical thrill and auricular fibrillation. Slight liver enlargement was present. This was the first she knew of her cardiac condition. Since 1929 she had been observed during several bouts of congestive heart failure and her response to treatment has been excellent. Electrocardiographic studies showed right axis deviation, inversion of all the T waves and slight depression of the R-T segments in the second and third leads.

Fluoroscopic and roentgenographic examination of the heart showed a triangular configuration. The left atrium was dilated, displacing the esophagus posteriorly and to the right. A large calcific deposit was seen within the left heart border, the point of greatest convexity being 2 cm. from the heart border. In the right anterior oblique position there was approximation of the most convex part of the calcific arc of the esophagus, the superior and inferior portions being separated from the esophagus. No elevation of the left main bronchus was present, and the two structures were visibly separated. Small calcific deposits were seen in the mitral leaflets.

Kymographic studies showed opposite pulsations in the calcified deposit in the left atrial wall as compared with the ventricle. The height of the ventricular waves was 1.0 cm. and of the atrial wave 0.3 cm.

DISCUSSION

The roentgenologic identification of left atrial calcification should not be difficult if the deposit is sufficiently dense. In the cases reported here the thickness of the calcification measured up to 2 mm. The

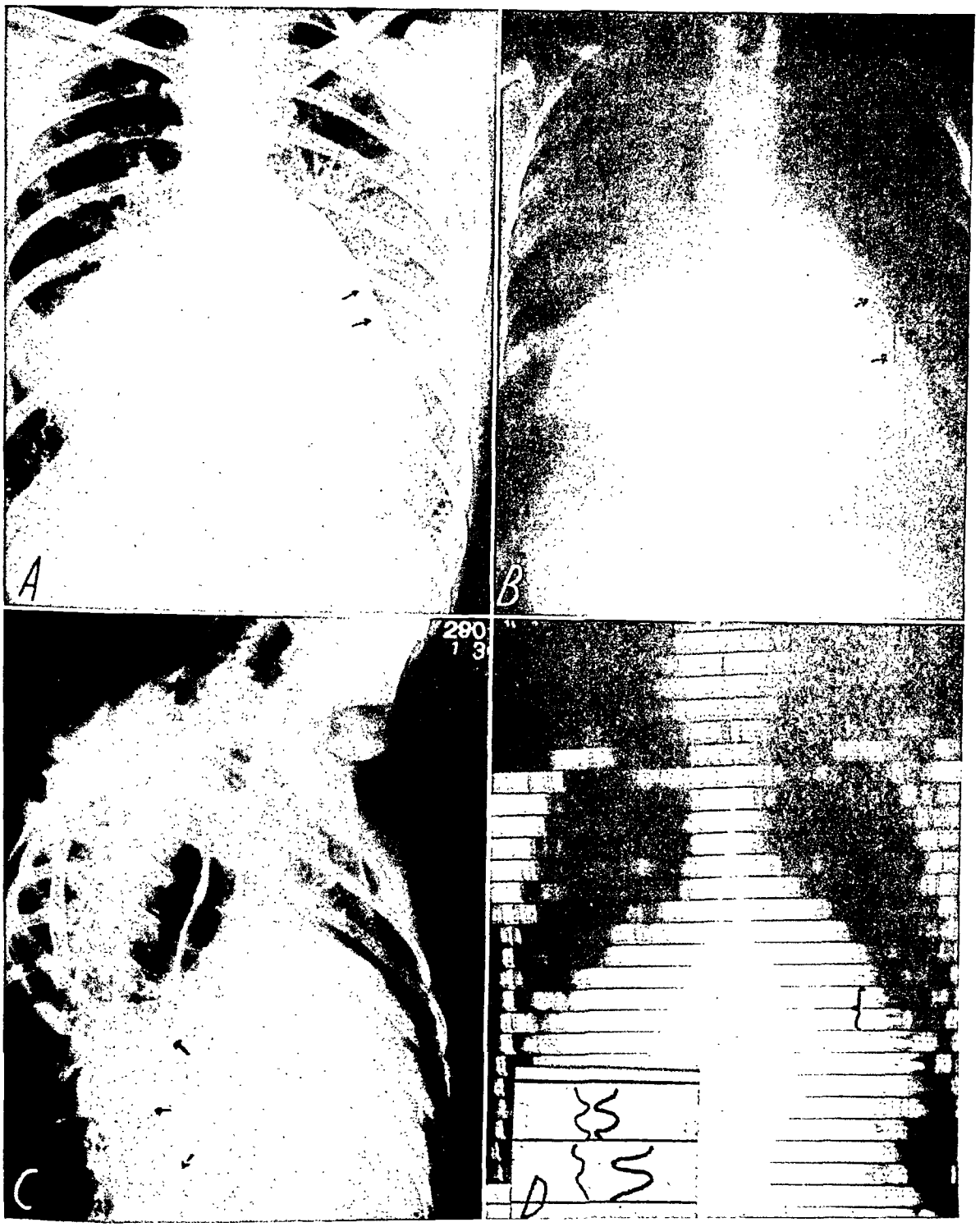


Fig. 2. Case II. *A*, teleroentgenogram showing faint calcific shadow at midportion of the left heart just within the border (black arrows). *B*, Potter-Bucky roentgenogram of the chest sharply visualizes the calcification in the left lateral aspect of the left atrium. *C*, right anterior oblique roentgenogram. The black arrows indicate the position of the posterior wall of the left atrium in relationship to the barium-filled esophagus. *D*, kymogram. The insert shows the opposing pulsations of the left atrial calcifications and the right ventricle.

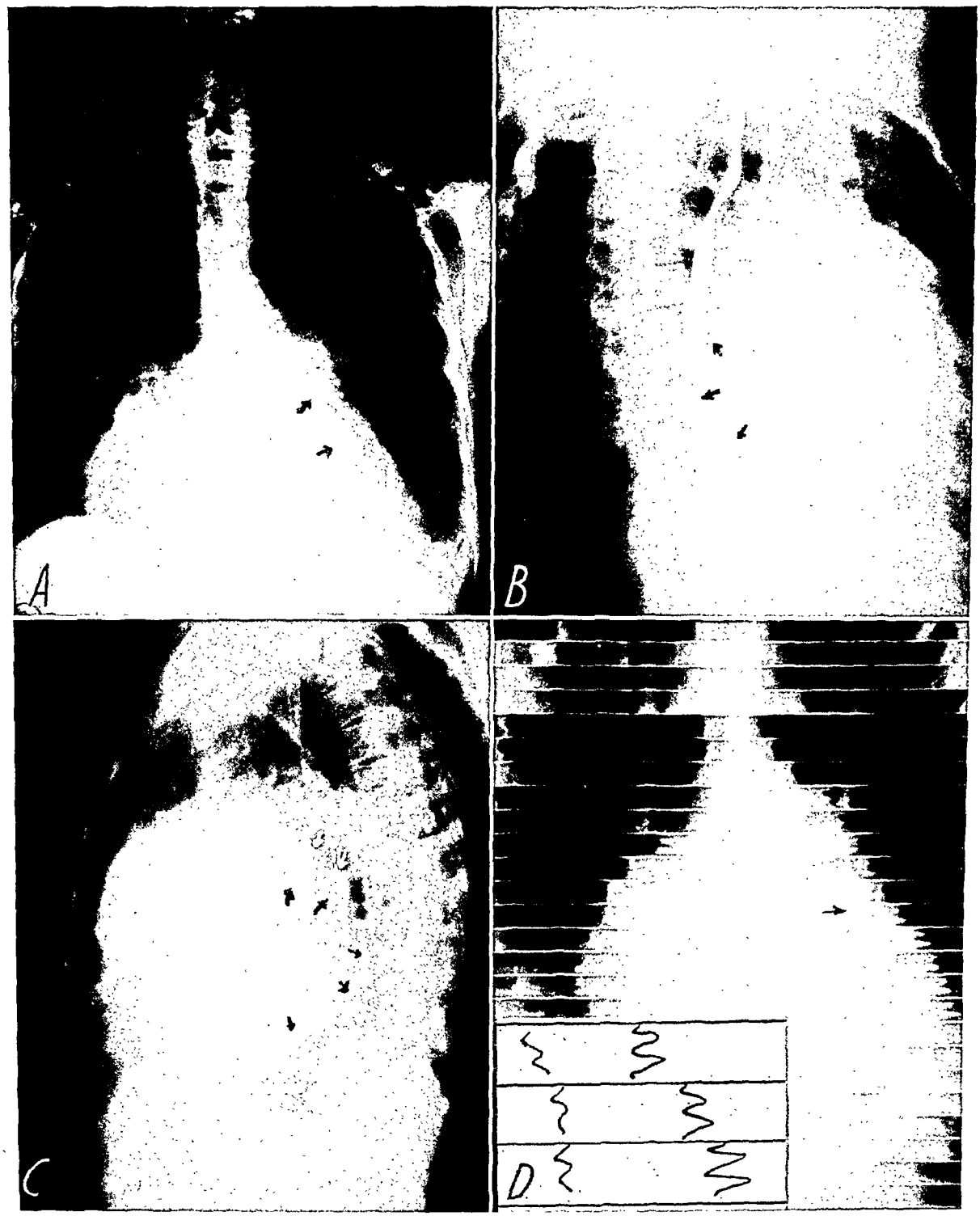


FIG. 3. Case III. *A*, overexposed teleroentgenogram showing left atrial calcification within the heart border. *B*, right anterior oblique roentgenogram. The arrows indicate the position of the posterior wall of the left atrium in relationship to the barium-filled esophagus. *C*, left anterior oblique roentgenogram. The left main bronchus (white arrows) is appreciably separated from the superior aspect of the left atrium (black arrows, upper). The posterior wall is indicated by the lower black arrows. *D*, kymogram. The opposing pulsations of the left atrial calcifications and the right ventricle serve to localize the calcifications.

heaviest deposits were on the posterior and the left lateral walls of the left atrium, and concomitant mitral valve calcifications were seen in 2 of the 3 patients. Begg also noted mitral valve calcifications in his patient. Roentgenologic study in the right anterior oblique position confirms the intimate approximation of the barium-filled esophagus with the posterior aspect of the left atrium, but this close approximation is present only at the point of greatest convexity of the dilated left atrium, giving one the impression that the indentation in the esophagus does not necessarily reflect the exact size of contour of the dilated atrium.

The relative positions of the left heart border and the left side of the left atrium are well demonstrated on these roentgenograms. Previous work on the outline of the heart based on postmortem findings has established the predominantly posterior position of the left atrium,[2,3,7,8] and this has been confirmed by more recent angiocardiographic investigations.[14] It is known that the left atrial appendage may become border forming on the left side of the heart. This structure, however, is of little importance in the reconstruction of the heart silhouette roentgenologically because it is relatively small, flat and contains very little blood. Rarely does the atrial appendage assume any function in the blood-containing capacity of the left atrium, even when the chamber is considerably dilated. It is realized, however, that infrequently the left atrium may become sufficiently dilated to appear on the left heart border.

The location of the calcification seen in the left atriums of the patients reported here reaffirm the fact that with dilatation of the left atrium the left heart border is not reached and that this chamber does not become border forming except in unusual cases.

There was no elevation of the left main bronchus in the 3 cases reported here or in Begg's case, indicating that this sign is not necessarily present with left atrial dilatation.

Differentiation of left atrial calcification from other cardiac calcification should be relatively easy. Valvular lime salt deposits may be identified by their intracardiac position and characteristic movements. Myocardial calcifications usually present an amorphous appearance which may vary considerably in size and position, and in questionable cases kymographic examination may prove helpful in determining the phases of contraction and relaxation of the heart muscle in relationship to the movement of the calcific deposit. Coronary artery calcifications as a rule are linear, small and may be rather difficult to identify. These may be seen in both the frontal and right anterior oblique positions at the left atrioventricular junction. Pericardial calcifications usually occur over the apex, the middle and lower segments of the left heart border or the diaphragmatic surface. When extensive the configuration of the pericardial envelope may be visualized. Fluoroscopic and kymographic examination may reveal diminished or absent cardiac pulsations. Echinococcus cysts of the heart with calcification are uncommon and the pattern would not be confused with left atrial calcifications. Calcification has also been mentioned with tumors of the heart, likewise a rare condition. Extracardiac and aortic calcification may be differentiated by careful fluoroscopic investigation.[12] Laminagraphy may aid in more sharply delineating calcific deposits, and spot roentgenograms are invaluable in making permanent records of fluoroscopic observations. It should be stressed that optimum ocular accommodation is essential, and the use of a small fluoroscopic field is of great assistance. The deposits are better seen roentgenographically on either overexposed films or on films made with a Potter-Bucky diaphragm. If the latter are desired a very short exposure is essential in obtaining adequate definition.

SUMMARY

Three patients with calcification of the left atrial endocardium outlining the cham-

ber to a greater or lesser degree are reported. All three were adult women with rheumatic heart disease and mitral stenosis and insufficiency. The left border of the left atrium was seen in each to be within the heart outline, establishing the fact that with dilatation of the chamber it does not become border forming on the left side of the heart. The impression of the posterior aspect of the dilated left atrium against the barium-filled esophagus in the right anterior oblique projection is due to close approximation of the chamber to the esophagus, but this relationship is present only at the point of greatest convexity of the dilated left atrium. Above and beneath the atrium is separated appreciably from the esophagus. The left main bronchus was not elevated in these three patients and an appreciable space existed between the two structures.

The endocardial left atrial calcifications are presumed to be due to lime salt deposits in MacCallum patches.

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VOL. 61, NO. 2

A CASE OF BRONCHIAL ADENOMA WITHOUT SIGNS OF BRONCHIAL OBSTRUCTION, CONCOMITANT WITH MINIMAL PULMONARY TUBERCULOSIS

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ABOUT two hundred cases of bronchial adenoma have been reported and several articles have been published treating the subject exhaustively. In all but a few instances some evidence of partial or complete bronchial obstruction existed. This case with no evidence of obstruction and the concomitant presence of a minimal tuberculosis created a difficult diagnostic problem which justifies recording.

CASE REPORT

A. M. R., white female, aged forty-six, came to the Outpatient Department of the U. S. Marine Hospital, Pittsburgh, Pennsylvania, on January 25, 1946, complaining of recent weight loss, chronic cough with yellowish sputum, occasional night sweats, pain in the chest, and one hemoptysis. Her mother had died a year previously of cancer. Her past history revealed right chronic mastoiditis and attacks of pain in the right upper quadrant of the abdomen, but nothing related to the respiratory organs; particularly, there were no repeated attacks of pneumonia. Physical examination of the chest was negative.

Stereoscopic films taken on January 26, 1946, showed small, sharply circumscribed, partially calcified areas of infiltration in the periphery of the second left interspace. The remaining portions of the lung fields were considered negative. The impression of the roentgenologist was that the lesion seen was apparently arrested and did not account for the hemoptysis. Close follow-up was advised. A blood count showed a moderate anemia, normal leukocyte count, and a sedimentation rate of 13 mm. Repeated sputum examinations were consistently negative; serial roentgenograms showed no change. During this period the patient felt essentially the same and continued to have occasional blood-streaked sputum. In June, 1946, on a roentgenogram (Fig. 1) inadvertently taken with a heavier technique than those taken previously, there was an area of infiltration about 1.5 cm. in diameter, somewhat rounded, not too clearly defined, seen about 5 cm. under the right hilum and partially overlapped by the right cardiac border. On the right lateral view the infiltration was thought to be below the hilum back to the

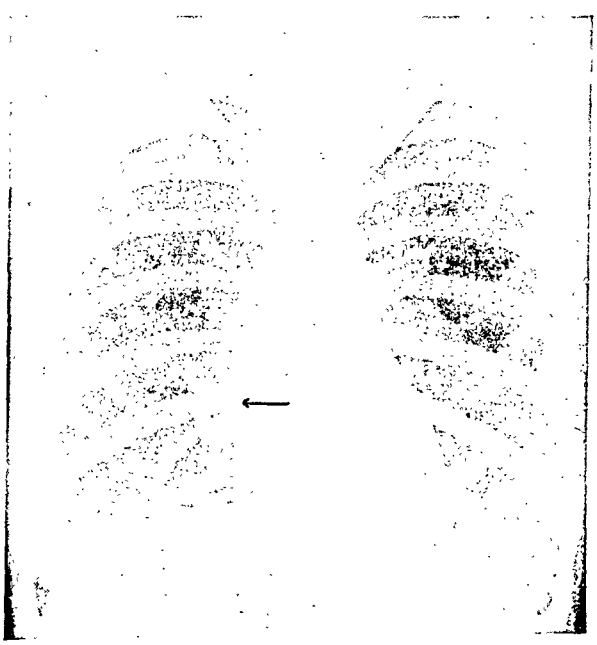


FIG. 1. Posteroanterior roentgenogram taken in June, 1946. One sees the small well defined areas of infiltration in the left upper lobe. There is at the apex of the angle made by the posterior aspect of the ninth right rib and the right cardiac border an area of infiltration about 1.5 cm. in diameter, somewhat rounded, not too clearly defined, partially overlapped by the cardiac border and the rib. The right lower and right middle lobes are entirely clear and there is no emphysema. (See arrow.)

fissure between the right middle and right lower lobes (Fig. 2). Neither of these lobes showed any evidence of obstructive emphysema, atelectasis, bronchiectasis, or chronic pneumonitis.

A review of the previous roentgenograms revealed that this infiltration had been overlooked and that it had not changed since January, 1946. Because of the nodular appearance, the stability and the location at the usual site of the contralateral spread of tuberculosis, it was thought that the area probably represented a nodular tuberculous infiltration, but since this type of tuberculous lesion is notoriously benign and not apt to produce hemoptysis, the possibility of a tumor was considered. At this



FIG. 2. Right lateral view. Below the hilum, back to the fissure between the right middle and right lower lobes is seen the area of infiltration. The right base is completely clear. (See arrow.)

time the patient ran a slight afternoon temperature and had a flare-up of the symptoms in the right upper quadrant.

She was admitted to the Marine Hospital. Several sedimentation rates ran between 10 and 15 mm.; the red blood cell counts were around 4 million with normal leukocyte counts and differentials. Sputum and gastric washings examined by smear, culture, and guinea pig inoculation were all negative for acid fast bacilli. A tuberculin test performed with 0.005 mg. Tuberculin Purified Protein Derivative was mildly positive. During her hospital stay the patient gained weight and her temperature returned to normal. On several occasions without apparent effort she brought up bright red blood from her mouth. Repeated chest examinations showed no change in either the minimal infiltration of the second left interspace or the somewhat nodular infiltration below the right hilum.

In view of this persistent hemoptysis and the failure to demonstrate any active tuberculosis, the probability of a tumor was more seriously considered. On October 8 a bronchoscopy was done and the larynx, trachea, and bronchial mucosa seemed to be a deeper pink than they would appear normally. There was no edema, ulceration, suppuration, or neoplasms throughout the tracheobronchial tract. It was suggested that if the symptoms persisted, another bronchoscopy be done.

The patient was then referred to the Tumor Clinic of the U. S. Marine Hospital, Baltimore, Maryland, where another bronchoscopy was performed. The following findings were seen: Approximately 3 to $3\frac{1}{2}$ inches from the carina, the right lower lobe bronchus appeared to be narrow, and immediately in front of the bronchoscope was visualized a rounded purplish mass which bled easily. The remainder of the bronchoscopy was negative. A biopsy was taken from the mass with the subsequent histopathological diagnosis of a bronchial adenoma. The patient was operated upon and a right lower and right middle lobectomy was performed. On the operative specimen, between the bronchus and the large vessel in the hilar region, there was a grossly lobulated yellow-gray tumor mass approximately 1.5 cm. in diameter. There was definite infiltration of the bronchial wall at the division of the right lower and right middle lobe bronchi. Microscopic examination showed rather circumscribed collections of basophilic cells in a scanty and loose fibrous stroma. These cells, which were uniform, exhibited indefinite cytoplasmic limits and deep staining nuclei of variable shapes. Each area of tumor had a compressed fibrous capsule. In one of the sections lung tissue was seen, and there was a localized area of fibrosis, necrotic in the center with infiltrated lymphocytes and compression of the lung parenchyma. The bronchial wall in some parts was edematous and contained collections of lymphocytes. The bronchial mucosa appeared normal. Pathological diagnosis: Adenoma of the bronchus.

COMMENT

Polypoid tumors of the bronchi produce bronchial irritation, partial or total obstruction, and bleeding. In these features

reside the explanation of the clinical and roentgenological picture. Consequences of slowly increasing bronchial obstruction are in almost all instances the predominant components of bronchial adenoma. Repeated attacks of pneumonia, obstructive emphysema, chronic pneumonitis, abscesses, atelectasis, and pulmonary fibrosis are usually present, alone or in various combinations.

In this case repeated slight hemoptysis, some cough, and apparently stable areas of infiltration were the only findings. As the infiltration of the left upper lobe was obviously tuberculous, the most likely diagnosis was tuberculosis with probable bronchial involvement to account for the hemoptysis. A tumor was considered the second choice. Undoubtedly, if there had been signs of bronchial obstruction in the segments distal to the right lower lobe with its nodular infiltration, the diagnosis of a tumor would have then been the diagnosis of choice.

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INTRALUMINAL DIVERTICULUM AND OTHER LESIONS PRODUCING INTERMITTENT DUODENAL OBSTRUCTION OR STASIS

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MORE and more attention is being given to the study of the small intestine. Improved methods for the examination of the jejunum and ileum include the fractional barium meal and intestinal intubation. These methods of examination have increased the diagnostic accuracy in the study of the small intestine. However, the radiologist should not consider the small intestine as a blind spot in the routine gastrointestinal series. It is rarely necessary to subject the patient to intestinal intubation in order to obtain an adequate study of the duodenum and jejunum. Routine examination of the stomach should always include one or more emptying films, and close attention to the passage of the barium meal through the duodenum and jejunum during roentgenoscopy should be considered an essential part of the examination.



FIG. 1. Arteriomesenteric occlusion of the transverse duodenum. The patient's colon and other organs were located quite low in the abdomen.

Extrinsic lesions producing deformity of the duodenum are relatively common. In our search for small intestinal pathology, we are more likely to find disease in other organs than in the intestine. This is particularly true of the second and third parts of the duodenum because of their intimate relationship with several neighboring structures. Brown and Harper[2] have recently

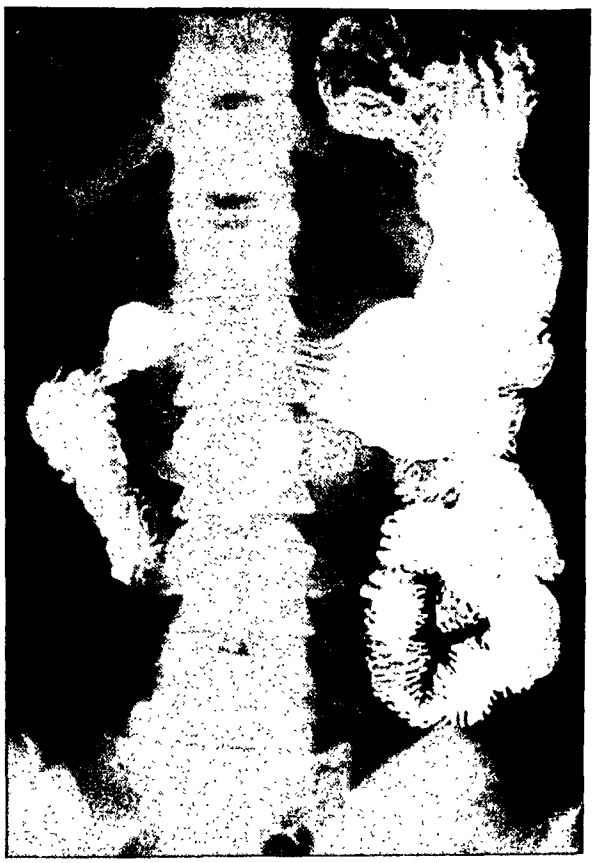


FIG. 2. Carcinoma of the pancreas. Metastatic glands at the root of the mesentery produced the stasis shown in this roentgenogram.

called attention to the importance of studying the duodenum in cases of extrahepatic biliary tract disease. They have found compression of the superior flexure of the second part of the duodenum a valuable sign in differentiating obstructive and non-obstructive jaundice.

Dilatation and stasis, confined to the first and second parts of the duodenum and the right half of the transverse duodenum, are characteristic of arteriomesenteric occlusion of the duodenum. The transverse portion of the duodenum is dilated on the right side of the spine and normal on the left side. This type of stasis is usually associated with generalized visceroptosis and should be suspected in individuals of the hypersthenic type who complain of nausea, pain in the epigastrium, and vomiting. Figure 1 illustrates this condition. The duodenal distention has caused some loss of the connivental markings in the descending part of the duodenum, although there is not an appreciable enlargement of the duodenal cap.

Pressure from an adjacent organ is perhaps more common than visceroptosis in the production of duodenal stasis. Because of its position, the pancreas is most likely to be the source of the pressure. Lesions of the head of the pancreas may produce the characteristic wide duodenal sweep and pancreatic carcinomas which metastasize to regional mesenteric glands can produce duodenal stasis much like that seen in arteriomesenteric pressure deformities of the duodenum. Figure 2 illustrates duodenal stasis secondary to carcinoma of the pancreas in a white female, aged thirty-five. A large sweep around the head of the pan-

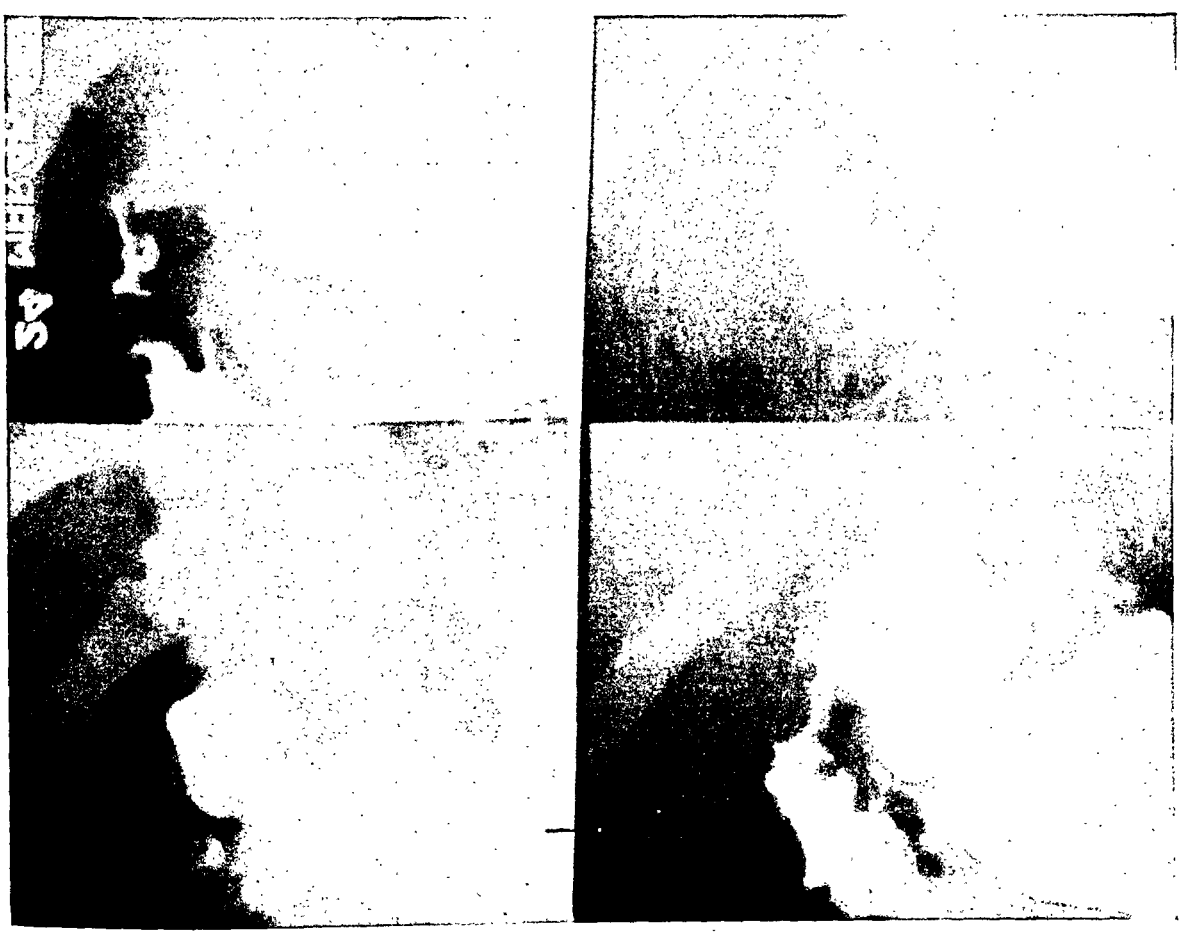


Fig. 3. Duodenal ulcer involving the lesser curvature of the second part of the duodenum. This patient was extremely refractive to all forms of medical management.



FIG. 4. Acute stomal ulcer at the site of an ancient gastrojejunostomy. This gastroenterostomy had functioned normally for twenty-five years.

creas is apparent, but the duodenal stasis seems to end at the vertebral border. The stasis was caused by metastatic glands at the root of the mesentery.

Intermittent obstruction and stasis are among the most common disorders seen in the distal portions of the duodenum, and if not due to extrinsic pressure may be the result of intrinsic pathology. Frequently, the first roentgenoscopic evidence of duodenal stasis is a dilated duodenal cap. If the distal loops of the duodenum are not dilated in the presence of megabulbus, careful attention to the descending loop of the duodenum may reveal acute ulceration. Figure 3 illustrates an active ulcer crater on the lesser curvature of the second part of the duodenum. Slight enlargement of the duodenal cap can be noted. There was a twenty-four hour gastric retention of almost 80 per cent of the barium meal.

Jejunal ulcers following gastrojejunostomy are relatively common. In some cases, these ulcers may cause sufficient spasm, or enough adhesions may form, to produce duodenal stasis or actual jejunal obstruction. Figure 4 shows an extremely dilated duodenum secondary to acute stomal ulceration at the site of an old gastrojejunostomy. This stasis was largely due to spasm, but surgical intervention was necessary to relieve the symptoms.

Foreign bodies occasionally obstruct the duodenum. Both tapeworms and roundworms have been responsible for obstructtion in this area. Toys and other foreign bodies swallowed by children either remain in the stomach, or if passed into the bowel, usually proceed on through the intestines and are eliminated. Figure 5 illustrates an unusual partial obstruction of the second part of the duodenum produced by a surgical sponge. The patient had sustained a gun-shot wound through the upper right abdomen which had perforated the duodenum. The lesion was repaired, and what seemed to be a good result was obtained. Several months later symptoms of partial



FIG. 5. Surgical sponge in the duodenum. Note surrounding inflammatory mass.

obstruction with elevation of temperature appeared. There was pain and tenderness in the epigastrium and on roentgen examination it was apparent that there was an inflammatory process in the region of the pancreas and second part of the duodenum. A laparotomy was performed and adhesions about the duodenum were freed. The bowel was not opened. Temporary relief was obtained, but after several weeks of observation it was necessary to operate again for relief of obstructive symptoms. The bowel was opened on this occasion and a surgical sponge was removed. Recovery was then uneventful.

Diverticula of the duodenum are quite common. They are most often seen on the lesser curvature of the second and third parts of the duodenum. They are not often symptomatic. They may be multiple and are frequently quite large. Both perforation and bleeding have been reported. Figure 6 shows an example of multiple diverticula of the duodenum in a patient who had a large esophageal hiatus hernia. In this case, the diverticula were completely asymptomatic, but the esophageal hiatus hernia was causing moderate epigastric distress. Some authors[6] believe that diverticulosis of the small intestine may produce epigastric distress possibly as a result of retention in the sacs. Edema and local swelling could conceivably produce stasis in the intestine.

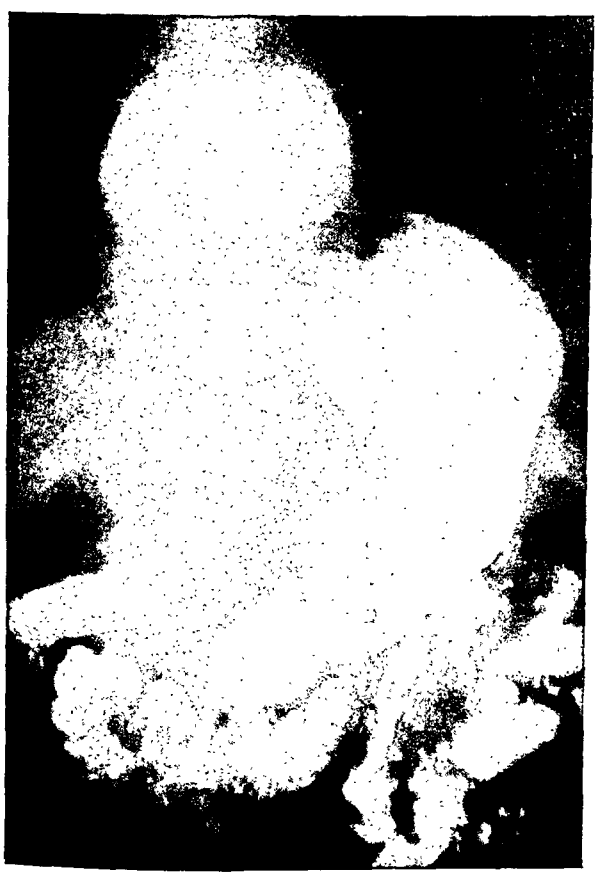


Fig. 6. Multiple diverticula of the duodenum in a patient with an esophageal hiatus hernia.



Fig. 7. Megaduodenum secondary to partial obstruction at junction of first and second parts of duodenum. Whether this obstruction is due to a partial intrinsic stenosis or to an extrinsic fibrous band is not known.

Megaduodenum may be secondary to vestigial intrinsic duodenal diaphragm.[3] These embryonic rests are quite rare and are seldom seen in adults. Duodenal obstruction in the newborn is still almost uniformly fatal although early diagnosis and surgery have recently begun to reduce the mortality.[4,5] Figure 7 is a roentgenogram of an adult white male who has a megaduodenum with an apparent partial stenosis or

perforate diaphragm at the junction of the first and second parts of the duodenum. Repeated roentgenoscopic examinations have failed to show any extrinsic pressure deformity and the partial obstruction is almost certainly intrinsic in origin. Although symptoms of distention and malnutrition have existed for years, the patient refuses surgical intervention and a more positive diagnosis has therefore been impossible.



FIG. 8. Case report. Roentgenogram made one hour after barium meal showing "gourd-like" sac in descending duodenum.

Intraluminal diverticulum of the duodenum has apparently not previously been reported. Bockus does not mention this condition.[1] An instance of intermittent duodenal obstruction produced by an intraluminal diverticulum, and proved surgically, is presented.

CASE REPORT

R. S., a white male, aged twenty-two, was admitted to an Army hospital feeling quite well. He gave a history of having had an acute attack of upper abdominal pain with vomiting and subsequent diarrhea while overseas on duty with the Armed Forces. A gastrointestinal examination at the time was reported as follows: "Duodenal obstruction probably secondary to extrinsic pressure." On careful questioning the patient admitted that he had had many previous episodes of nausea, vomiting, and diarrhea over a period of many years. The first attacks occurred in early childhood. Recovery from previous attacks had usually taken place in two or three days with no particular treatment except bed rest. Physical examination and routine laboratory examinations were negative. Roentgenoscopic examination of the stomach revealed a megabulbus, but the distal part of the duodenum seemed quite normal. A film made one hour after the barium meal showed a gourd-like structure, partially filled with barium, in the descending duodenum. Subsequent films failed to demonstrate the structure again, and in five hours the stomach and duodenum were empty. After a few days the examination was repeated. The duodenal bulb was greatly dilated and as barium entered the descending duodenum it was seen to fill a sac-like structure which enlarged and completely obstructed the duodenum. It was impossible to force any of the barium beyond this point. After manipulation and palpation, the sac was emptied by milking the contents back into the stomach. After emptying of the sac, barium was seen to pass around it and proceed on through the distal loops of the duodenum in normal fashion. A diagnosis of intraluminal diverticulum of the duodenum was made. Surgical exploration confirmed the roentgen diagnosis. The sac was found to have a mucosal lining on both the inside and outside. It was possible to invert the sac in the manner of turning the fingers of a glove inside out. The mouth of the sac was located just distal to the vaterian area. Figures 8, 9, 10 and 11 illustrate the roentgen findings.

COMMENT

Duodenal obstructions are seen in all age groups. Those occurring in early life are usually due to congenital malformations. These malformations may be intrinsic or extrinsic in nature. They are called intrinsic when the obstruction is due to a perforate or imperforate diaphragm, when partial or subtotal stenosis is present, and when there is an atresia.[4] Figure 7 illus-

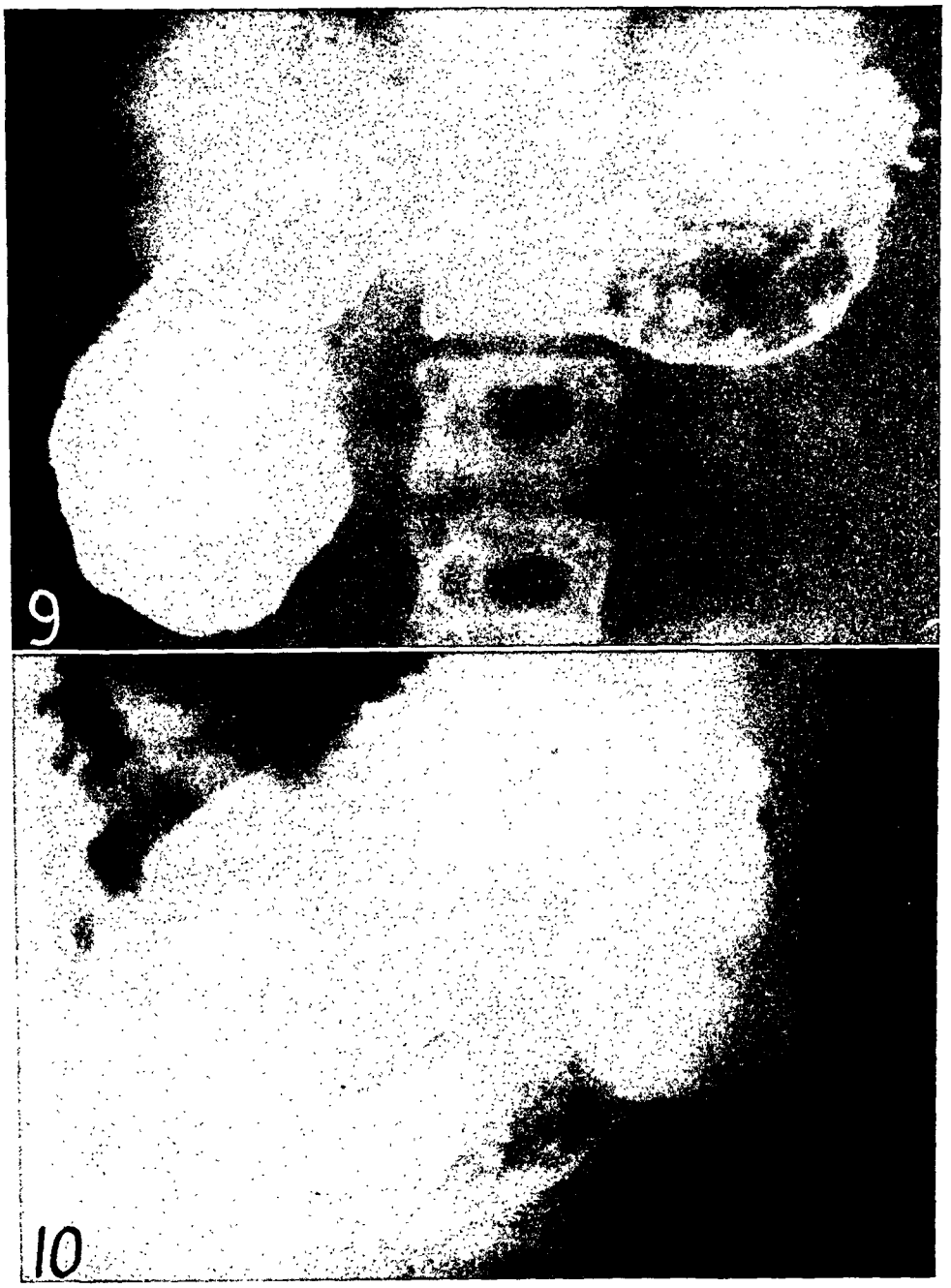


Fig. 9, 10. Case report. Spot roentgenograms in anteroposterior and right lateral projections showing intrinsic diverticulum well filled with barium and completely obstructing duodenum.

trates a case which falls in the group of intrinsic obstruction due to a partial stenosis. This patient has refused surgery and has shown some improvement on medical treatment. Nine cases of intrinsic duodenal diaphragm have been reported in the literature.[3] This persistent structure is a result of incomplete recanalization of the fetal duodenum. During early fetal life the duodenum becomes completely obliterated by epithelial proliferation. At this stage in development, the pancreatic and hepatic ducts are being formed.[4] Normally, the duodenum is then recanalized and complete re-establishment of the duodenal lumen takes place. It seems logical to assume that an intrinsic diverticulum in the duodenum could result only secondary to



FIG. 11. Case report. Spot roentgenogram of partially evacuated sac showing presence of mucosal folds. After evacuation of the sac, barium passed around the diverticulum and proceeded normally through the bowel.

some remnant of a duodenal diaphragm. Our patient's history of intermittent obstruction in early life would seem to indicate that his duodenal deformity was congenital in nature.

SUMMARY

1. Duodenal obstruction and stasis have been discussed, and several of the more common causes have been presented and illustrated.

2. A case of intraluminal diverticulum of the duodenum, producing intermittent obstruction, is presented.

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THE ROENTGEN MANIFESTATIONS OF PANCREATITIS COMPLICATING MUMPS

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IN PREVIOUS papers on the roentgen manifestations of pancreatic conditions mumps could only be mentioned and illustrated briefly. It is the purpose of this paper to enlarge upon the subject.

Mumps is a general, specific, infectious disease with characteristic localization in the parotid and other salivary glands. Among the common complications are orchitis, oophoritis and mastitis.

Accompanying some of the typical cases is a clinical syndrome which is characteristic of pancreatitis, either in the acute or subacute form. The latter is the more common form. The condition is rarely serious.

In the acute form there may be high fever, nausea, vomiting, severe pain over the epigastrium and left hypochondrium with radiation towards the back, developing some prostration usually, but not always, about one week after the onset of the parotid swelling. The urine may contain sugar. On physical examination there is tenderness over the pancreas with some overlying muscular rigidity.

In other cases the pancreatitis is mild with only a slight to moderate degree of the above symptoms and signs.

The pathological changes are:

1. Gross
 (a) swelling of the pancreas with redness.
 (b) enlargement with congestion of the adjacent lymph nodes.
2. Microscopic
 (a) congestion of the blood vessels.
 (b) edema and swelling of the cells of the external secreting glands, as well as of the islet cells.
 (c) cellular infiltrations, chiefly mononuclear, occur.

ROENTGEN STUDY

The roentgen examination consists of roentgenoscopy, simple preliminary films and barium meal study.

The roentgen signs of acute pancreatitis are:

Marked intolerance to barium in the duodenal loop with or without enlargement and displacement of the loop. The loop is so irritable that it is difficult to visualize any barium therein. It resembles the intolerance seen in the Stierlin phenomenon in cecal tuberculosis.

Elevation of the stomach.

Restricted motion or freezing of the left diaphragmatic dome.

Transverse position of the duodenal bulb with or without enlargement of the duodenal loop.

Collection and stasis of appreciable quantities of contrast material in the dependent portions of the duodenum.

Fullness between the transverse colon and the stomach.

Ill defined left psoas muscle contour.

Pressure indentations on the stomach and duodenum.

Coarsely feathered duodenal mucosal relief, possibly due to edema.

Abnormal gas distention of the colon, especially the transverse portion, and even a paralytic ileus with the formation of fluid levels when the patient is examined in the erect or lateral recumbent posture.

The roentgen manifestations of the subacute forms may vary from no demonstrable manifestation to slight or moderate degree of the manifestations described under the acute form.

INCIDENCE

Ninety-five (65 male and 30 female) con-

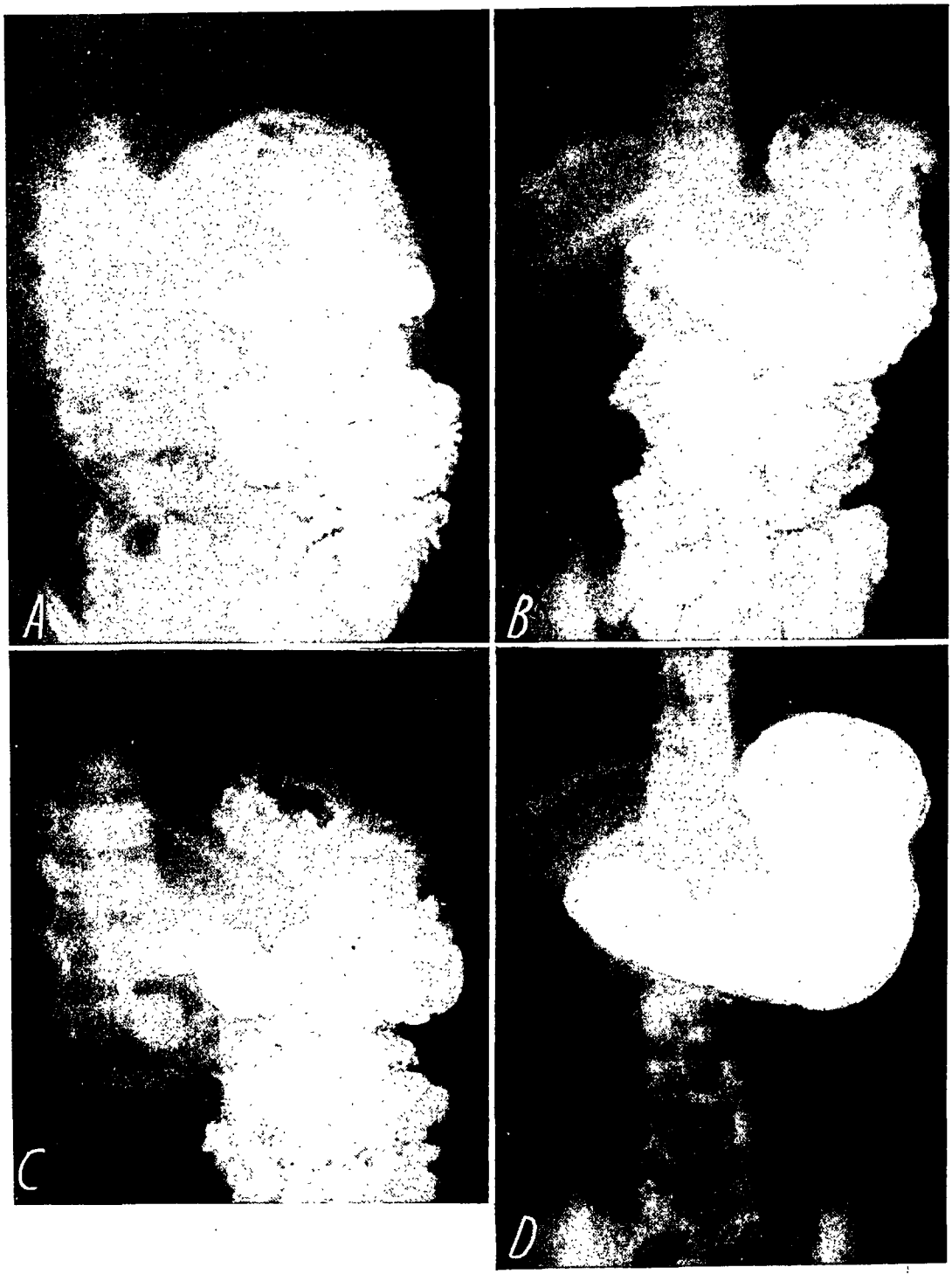


FIG. 1. *A, B, C, D.* Case 1. Elevation of stomach and bulb; marked duodenal intolerance to the barium sulphate.

secutively diagnosed cases of mumps in patients up to the age of thirty were available for study. Of these, 17 (15 male and 2 female) had signs and symptoms referable to the pancreas and were classified clinically as follows: acute pancreatitis, 3 (2 male and 1 female) and subacute pancreatitis, 14 (13 male and 1 female).

The 3 acute and 11 of the 14 subacute cases were roentgenographed. All 3 of the acute cases, in patients four, nine and ten years of age, were definitely positive. Of the

11 subacute cases roentgenographed, 4 were normal and 7 showed positive findings.

The 3 acute cases (Fig. 1, 2 and 3) and 1 of the typical subacute positive cases (Fig. 4) are herein described. No special sequence nor interrelationship with the other more common complications was discernible.

CASE REPORTS

Case 1. The patient, male, aged four, vomited twice and refused food on the sixth day following the onset of parotid mumps. The tempera-

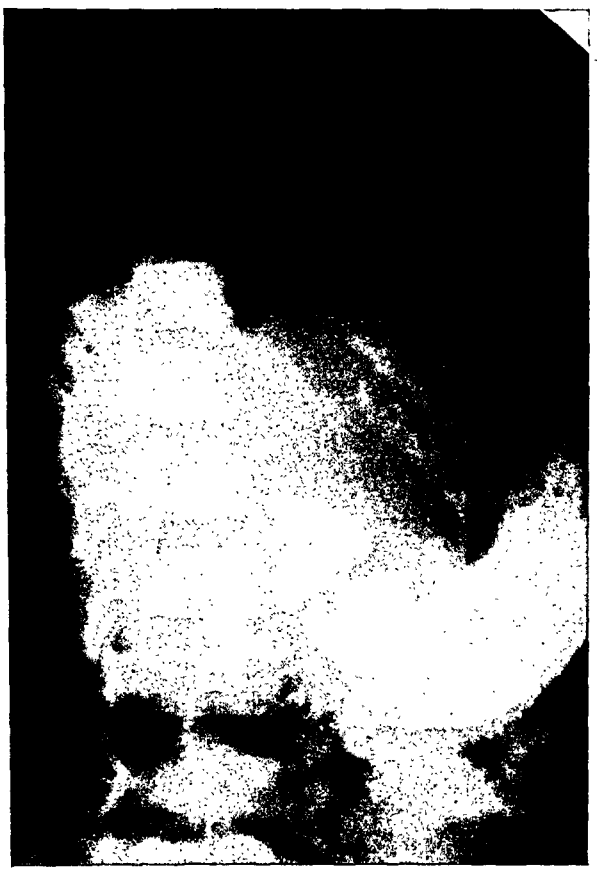


Fig. 2. Case 11. Moderate duodenal intolerance to the barium sulphate; coarsening of the duodenal mucosa.

ture was 104° F. There were no other complications. The roentgenoscopic and film studies (Fig. 1) revealed marked duodenal intolerance to the barium sulphate, with pancreatic tenderness roentgenoscopically. The stomach and bulb were elevated. The movement of the left



Fig. 3. Case III. Marked duodenal intolerance to the barium sulphate.



Fig. 4. Case IV. Moderate duodenal intolerance to the barium sulphate.

diaphragm was restricted. The duodenal loop was not perceptibly enlarged.

CASE II. The patient, male, aged ten, complained of epigastric pain eight days after the onset of parotid mumps. There was nausea and vomiting. The temperature was 103° F. There were no other complications. The roentgenoscopic and film studies (Fig. 2) were similar to the above except that the duodenal intolerance to barium was not as marked. This permitted visualization of the duodenal mucosa, which was coarsened.

CASE III. The patient, female, aged nine, complained of pain in the epigastrium and left hypochondrium beginning six days after the onset of parotid mumps. The temperature was 102.2° F. There were no other complications. There was loss of appetite and slight nausea but no vomiting. The roentgenoscopic and film studies (Fig. 3) revealed marked duodenal intolerance to the barium sulphate and pancreatic tenderness roentgenoscopically. The duodenal loop was not enlarged.

CASE IV. The patient, male, aged thirty, complained of vague mid-abdominal and back pain ten days after the onset of parotid mumps. The temperature was 100° F. There was continued slight nausea and anorexia but no vomiting. The roentgenoscopic and film studies (Fig. 4) revealed to a slight degree the signs described under the acute cases. The most constant roentgen finding was moderate duodenal intolerance to barium. There was no tenderness and no enlargement of the duodenal loop.

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DEMONSTRATION OF SINUS TRACTS, FISTULAS, AND INFECTED CAVITIES BY LIPIODOL*

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Medical Corps, Army of the United States

THE purpose of this paper is to present the technique of the injection of sinus tracts, fistulas, and infected cavities. The justification is the scarcity of literature on this subject, the fact that by the information gained curative procedures are instituted at an earlier date, and that the surgeon explores with preoperative knowledge of the extent and direction of the disease process.

One of the few articles in the literature is that by Gage and Williams[1] of the Radiological Department, St. Mary's Hospital, London, England. This article was of such exceptional merit that it was republished in full in *Radiology*. It will be quoted freely in this paper.

A sinus is a tract leading from the skin or mucous membrane to a deep-seated focus of suppuration, a vestigial structure, or an aberrant secreting tissue.

* From the Battey General Hospital, Rome, Georgia.

[1] Gage, H. C., and Williams, E. R. Radiological exploration of sinus tracts, fistulae and infected cavities. *Radiology*, 1943, *41*, 233–248.



FIG. 1, *A* and *B*. Case 1. This illustrates a cavity in bone filled by the replacement method. The sinus had drained for six months. Very little evidence in the plain film. Very small opening in the skin. A few minims of lipiodol were injected and the pressure was too great for further injection. The syringe was removed and pus exuded. This was repeated twelve times with the heavier lipiodol sinking to the bottom and displacing the pus. At operation a large cavity as shown was unroofed, and in a few weeks the patient's drainage stopped.



Fig. 2. Case iv. A Y shaped sequestrum with five sinus tracts leading through bone to skin openings. Four of these openings had to be plugged. It is readily apparent in this case that the operative approach can be planned so that the continuity of bone is not completely interrupted. If the operation is not planned with this in mind, a fracture may occur which in this sclerotic bone may result in non-union or in marked delay in union. Operative removal of the sequestrum was performed. No drainage now for three months.

A fistula is an abnormal tract leading from a mucous surface to another mucous surface or to the skin.

The walls of chronic sinuses are made up of fibrous tissue lined by granulation tissue which constantly produces pus. In very long standing sinuses and fistulas there is usually a down growth of epithelium from the skin or mucous surface which may become complete and prevent closure of the abnormal tract.

Persistent tracts are due to: first, and most important, the presence of sequestra or foreign bodies; second, inadequate drainage; third, epithelization of the tract.

Generally speaking, the principles of treatment of sinuses and fistulas are two in number. First, the necrotic or foreign material must be removed and adequate drainage provided. Second, if the tract persists after removal of the cause, then the tract must be removed or destroyed.

The injection and roentgenological demonstration of sinus tracts, fistulas, and abnormal cavities is by no means simple. The prime requisite is to have the sides of the injection mechanism tightly applied to the walls of the tract and still have the tip free, that is not in contact with the underlying structures. This has been the main problem as we have met with every conceivable type of opening. The pin-point opening is injected best by an ordinary No. 20 gauge needle with the shaft cut off near the base. As this has a sloping smooth enlargement from tip to base with a smooth blunt tip it is more efficient than the lacrimal duct cannula advocated by Gage and Williams. For a slightly larger opening the shaft is pulled out of the base with a pair of pliers. We do not have the special conical rubber adaptor nozzle used by Gage and

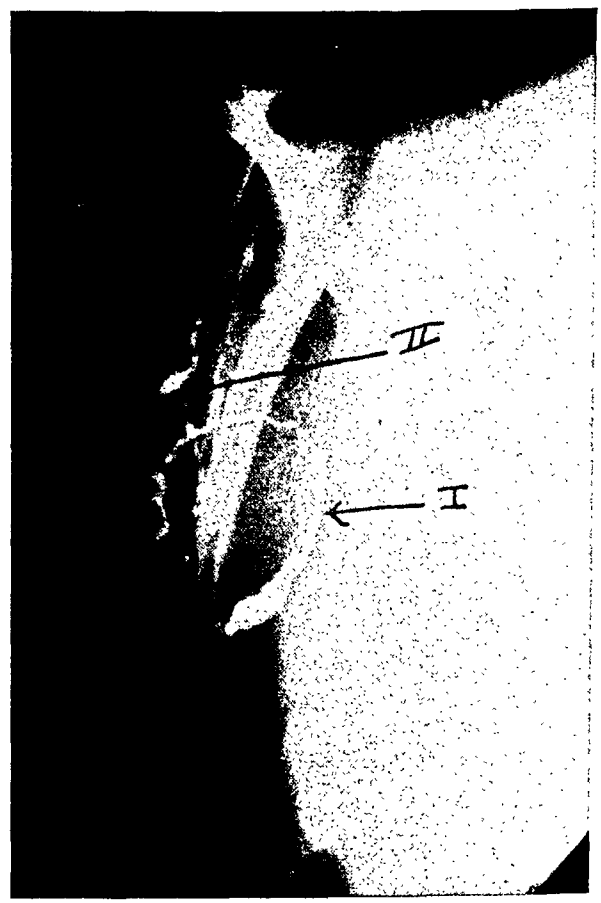


Fig. 3. Case v. (*I*) A long curving tract ending in a surface defect in bone near the lower angle of the scapula. (*II*) A second tract leading along a surface defect on the posterior surface of the scapula. Both tracts are inadequately drained.

Williams, but have used an improvised one which has certain advantages, namely, the tip lies away from the end of the rubber adaptor. These are easily made from the stoppers used on nearly all standard rubber capped vials. The stopper is inverted and a hole cut in the part that projected into the vial. This is pulled up on the metal adaptor of an ordinary syringe. This has made injection of tracts possible when other methods have failed.

A second improvised injector that has been of value is made from the rubber cap of a medicine dropper. The open end is cut off and an opening made in the closed end. These openings are of various sizes and are slipped over either the needle base or the metal adaptor of a syringe. This gives an efficient conical rubber injector. Telescoping or fitting one of these dropper caps into another and slipping them over the needle base or metal adaptor makes a pliable injecting mechanism with a protected tip which can be used to advantage.

Injection through an inserted catheter is necessary in some of the gaping wounds. The danger in this is that a superficial tract may be by-passed. I believe that the ideal injecting mechanism for a number of the openings would be one suggested by Colonel Faust of this station. This utilizes cannulas of various sizes threaded through solid rubber balls of various sizes. If these were available, lipiodol injection would be very much simplified in some cases. After insertion of the injecting mechanism, if the injection is difficult, the tip is tilted up, down, or to the side. It is necessary in

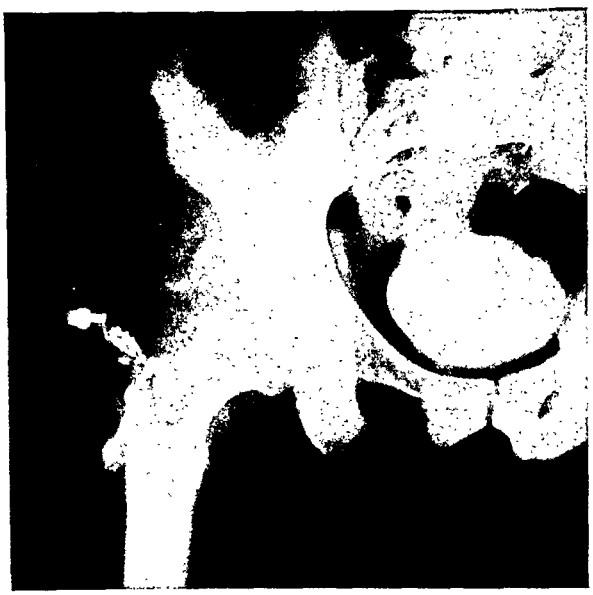


Fig. 4. Case vi. A cavity between fragments with tracts leading into a large cavity in the head of the femur. Operation—Multiple small hard fragments of bone found in a cavity in the head and neck. Cavity admitted a finger and was smooth walled.

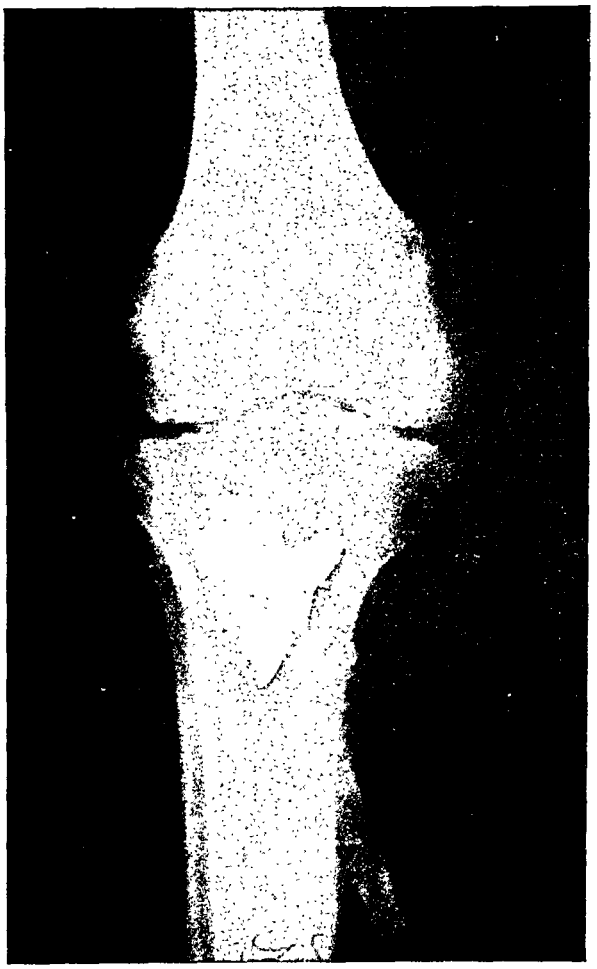


Fig. 5. Case vii. A chronic bone abscess not the result of trauma. Drainage of seven months' duration. Very difficult to inject. The tip would always strike an obstacle that would plug it. Shifts of position would not allow injection. Only by using a protected tip could the injection be done and then only by using marked pressure alternation with suction. There must have been a piece of tissue acting as a ball valve with obstruction to the inflow as this cavity was draining freely. At operation the cavity was unroofed and curetted. Much dirty granulation tissue was removed. This lesion was supposedly secondary to a gonococcal arthritis of the knee.



Fig. 6, *A* and *B*. Case ix. Plain film revealed a cavity in the left ilium containing a metal fragment. This was evident as the cause of drainage. Lipiodol injection was needed to rule out other pieces of metal acting as foci. Operation—Removal of metal fragment and adequate drainage of cavity. No drainage for the past six weeks.

tracts with multiple openings to plug several or all but one in order to reach all of the extensions. This is most readily accomplished by pressure of a gauze covered finger or fingers. Collodion has not been used since the method described when assistants are available is so simple.

In private practice I twice made use of a purse string suture, drawing the skin itself up around the syringe. This was the only way that I was able to inject one tract in the loose scrotal tissues.

The utilization of gravity has been of value in many cases with films taken at intervals.

Lipiodol has been the injected material used here. To conserve lipiodol we have been able to determine the amount of lipiodol which we will need in the syringe



Fig. 7. Case xiii. Cavity in the os calcis. Plain film very indefinite. Marked pressure alternating with suction was necessary to fill the cavity. Operation —Removal of three sequestra and considerable granulation tissue.



Fig. 8. Case xiv. Cavity in badly comminuted fractures of the tarsal bones. The cavity or tract involves the calcaneocuboid and the anterior subastragalar joint. Tract traverses the length of the os calcis and emerges posteriorly. There is a lateral extension. Operation—Cavity unroofed. Sequestra and granulation tissue removed. Patient has had no drainage for two months. Arrow points to the rubber cap protecting the tip of the injecting mechanism. This rubber cap is indispensable in the injection of certain types of tracts.

by the amount of drainage. This has been a correct estimate in a great percentage of cases. It is best to have too much in the syringe as its removal for filling causes spillage from the opening in the skin or mucous surface. At times in large cavities it might be advisable to mix the lipiodol with equal parts of sterile olive oil. Lipiodol appears to have some therapeutic value of its own as many cases have had a cessation of drainage after injection.

The question of how much pressure to use in a given case is most difficult. There have been cases of lipiodol passing into the



Fig. 9, *A* and *B*. Case xvii. A cavity in the lateral condyle of femur and adjacent tibia. If this patient is ever to be treated by arthroplasty, then complete eradication of the cavities is probably indicated. There are many cases with cavities very near or actually bulging beyond the articular surface of bone. Many of these have spontaneously closed. Some have remained closed and others have reopened.



FIG. 10. Case XVIII. Cavity in the ilium at edge of acetabulum connecting with the joint cavity. Note lipiodol outlining the joint capsule. No ill effects from this. This is not desirable, but could hardly be avoided in this case. This film made twenty-four hours after injection. Films made one week later showed considerable absorption of lipiodol from the hip joint?

veins draining the uterus in hysterosalpingography, but no serious effects have been noted from this. I had this happen in one hysterosalpingogram and have films showing the lipiodol in the iliac veins. There was mild shock but no ill effects. This probably would not happen in these cases because of the surrounding fibrosis. I do not hesitate to use marked pressure alternating with release of pressure to introduce the first cubic centimeter as there are often little plugs that may act in a ball valve manner or may simply plug the opening. After this point is passed then undue pressure should not be utilized.

Fractional injection in one bone cavity was valuable. This patient had a pin-point opening and a few minims of lipiodol raised the pressure so that more force was inadvisable and also impossible. The injector was removed and pus came out. This was repeated ten or twleve times with the heavier lipiodol displacing and expelling the pus until a large cavity was filled.

In a mass of granulation tissue the point of exit may be determined by pressure. At one point a drop of pus will exude pointing to the likely injection site. At times small sequestra in the tract will interfere with injection and have to be removed.

After injection the problem of retention of the medium during film examination is usually met by having the patient or ward man hold the syringe or by holding the syringe by sandbags. Both have been used and both are satisfactory with the former much simpler. A frequently used method of retention of the lipiodol is by sliding a

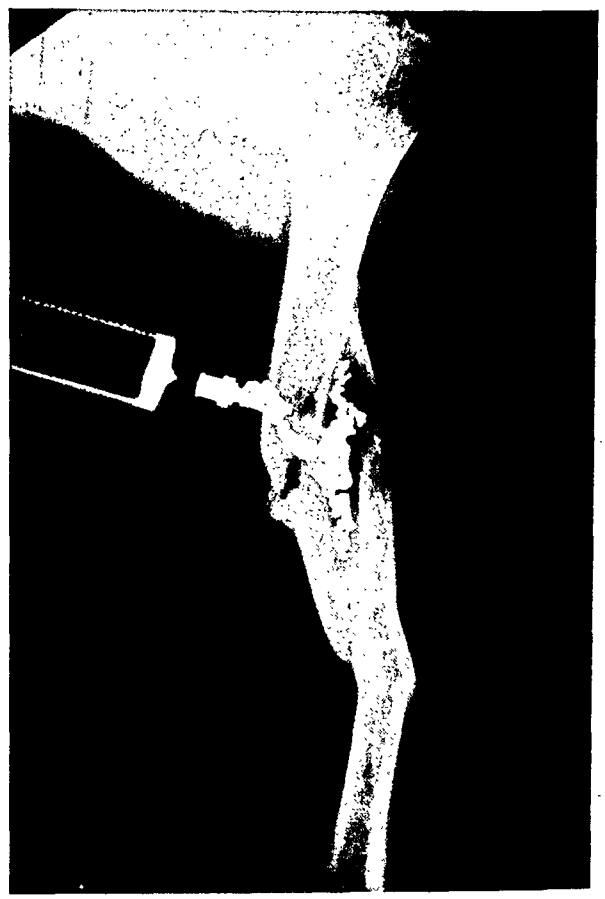


FIG. 11. Case XIX. Cavity between fragments. No sequestra or foreign bodies. Cavity only three-fourths surrounded by bone as shown by multiple views. It appears that this type of cavity only partially surrounded by bone tends to heal spontaneously when no foreign material is present. These act about the same as soft tissue cavities.



FIG. 12. Case XX. *A*, lipiodol fills a large cavity in the left abdomen. Healing comminuted fracture of the body of the third lumbar vertebra. *B*, illustrates the use of gravity. Patient was turned on right side for several hours. Lipiodol fills a large cavity in the body of the third lumbar (arrow) and passes to the right to fill a cavity containing the large fragment of metal.

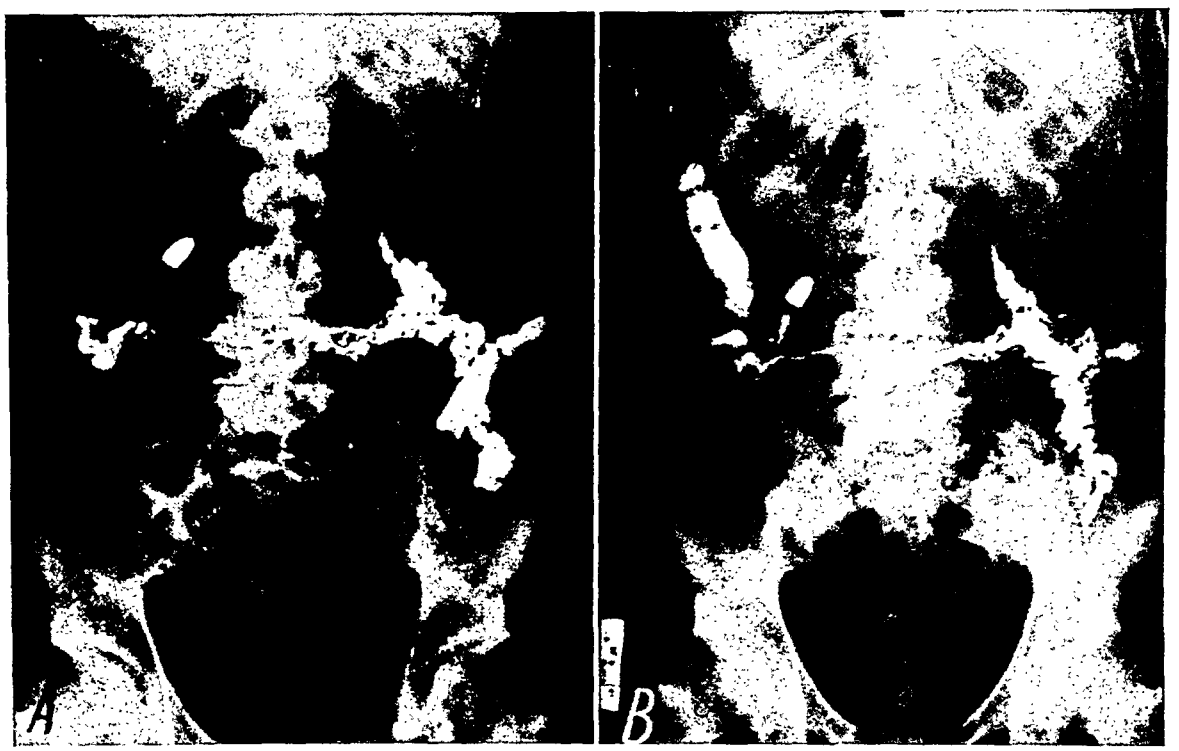


FIG. 13. Case XXIII. *A*, long complicated tract through the body of the fourth lumbar vertebra. Arrow points to a shadow resembling a drainage tube. This shadow represents the site of a tube that had been in place for several weeks. Twenty cubic centimeters of lipiodol was used and the patient turned on his abdomen for twenty-four hours. No bowel connection was demonstrated. The metal foreign body is on the left side. *B*, on second injection 35 cc. of lipiodol was used. The tract connected with the descending colon lateral to the bullet. There was also a connection with the ascending colon near syringe tip. Only a very small amount entered the ascending colon and a large amount the descending colon. The lipiodol also gravitated to the bullet.

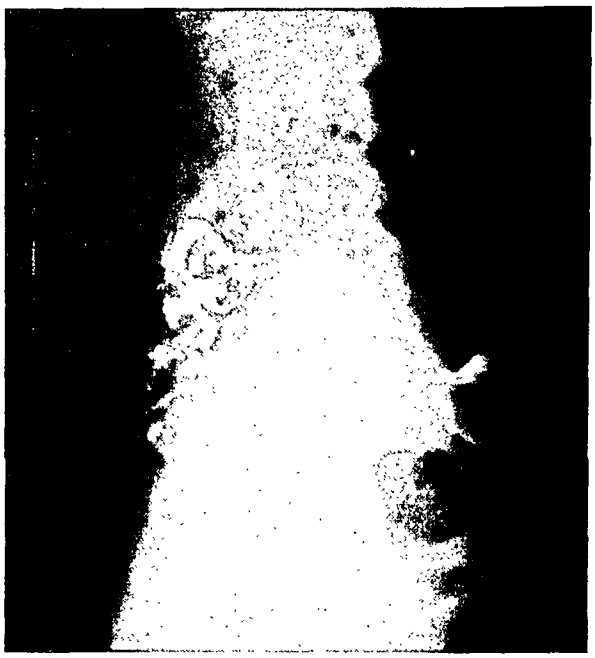


FIG. 14. Case XXVI. A tract leading from a posterior opening through a cavity in the right sacroiliac to enter the cecum. There is also a fistula from the anterior abdominal wall to the cecum. Internal fistulas leading from bowel to bone must always be correctly evaluated. It would do very little good to saucerize and curet a cavity that is being fed by colon contents. Odor is no criterion of connection with bowel. Fecal drainage has not been observed. The fistula to the bowel must be repaired first, and then the bone abscess treated. Connection with the bowel can be demonstrated with methylene blue by mouth, but the location cannot. Operation—Fistulas disconnected and bowel repaired. Bone focus to be operated on if drainage continues.

gauze covered finger quickly over the opening as the injecting mechanism is removed. This is especially easy when the pliable rubber mechanism is used. In the illustrations it will be seen how little the fingers and hands interfere with detail. It is easy to slide a piece of clean dry gauze in place of the one plugging the opening without spillage. This prevents confusing shadows from any initial leakage.

It is surprising how little evidence there may be on the plain film of a cavity in bone. Sclerosis around a defect is not an indicator as this may occur around a defect by chemical or thermal irritation from the passage of metal through bone. Also the sclerosis may be so slight that it is not visualized.

Plain roentgenograms should always be made before injection.

Roentgenograms should always be made even when there is apparently no chance of enough lipiodol entering to be of any value. We were agreeably surprised in several cases. Large films should be taken whenever a tract around the trunk is investigated. One word about technique may save re-examinations. It is advisable to routinely add 5 kv. to the regular technique.

Stereoscopic roentgenograms are imperative in complicated tracts. To these should be added a film made at a right angle to the stereoscopic projection. Oblique films are at times necessary. Anteroposterior and lateral views are usually sufficient.

So far as I know there are no contraindications to the injection of lipiodol into a sinus or fistula except an acute or subsiding acute inflammatory process. Complications so far have had no serious after effects and have been limited to 3 cases. Two cases with abscess cavities in the upper end of the tibia near the knee joint had febrile reactions with chills and some swelling of the joint. Both recovered quickly under sulfonamide therapy. The third case



FIG. 15. Case XXVII. Soft tissue abscess ruling out bone focus. Operation—Incision of cavity with removal of a piece of canvas legging. No drainage now.

showed a connection with the hip joint, but no ill effects. The patient has almost complete range of motion of this joint with very little pain. Some local minor flare-ups have occurred consisting of slight soreness for twenty-four hours.

Everyone is familar with the long history of chronic osteomyelitis with its quiet periods and apparent healing followed by flare-ups and further drainage. These post-traumatic cases seem to present a different picture roentgenologically. This series presents less sclerosis and thickening of bone around the cavities. Perhaps this will come in time as these cases are much earlier than those usually seen in private practice. The mechanism of production of the two is different. The former is a pressure and inflammatory necrosis from within, the latter from without, establishing a tract at the onset. Many of these cases close spontaneously. Many reopen and drain while the patient is still in the hospital. The question I would like to raise is whether every draining sinus of more than one month's duration should not be injected fairly early and whether or not on demonstrating a cavity this should be opened, curetted, and adequately drained, providing of course, that there is enough bone support for union. These spontaneously closed cavities may in later years be caused to flare up by trauma or by some debilitating disease. At present the policy is to inject all draining sinuses of a month's duration. It can probably be stated without exception that any cavity containing a foreign body either bone, metal, or other material should have that foreign body removed.

The cases illustrated have been taken from the 150 cases injected from January, 1943, through April, 1945, in the Department of Roentgenology at Battey General Hospital. Many interesting cases have been omitted because of space requirements. Many lateral or anteroposterior views have been omitted for the same reason. Since the completion of this paper we have had one case of a type not shown in the illustrations included here. This sinus passed in from the left flank to connect with a large metal foreign body in the body of the first lumbar vertebra. From the middle of the tract there were two connections with the kidney.

CONCLUSIONS

1. Many uninfected defects in bone as the result of penetrating metal show a surrounding zone of sclerosis. Many other cases have foreign bodies in the soft tissues and bone. The continued drainage may be due to either the foreign body or the cavity in bone. Lipiodol will usually determine which or both.

2. There are many infected cavities in bone which have an internal connection with the bowel. It is probably always correct to repair the fistula first.

3. Cavities near or in joints probably require treatment if these patients are to be treated later by arthroplasty.

4. It seems that the optimum time for operative interference is as soon as the bone is strong enough to prevent fracture. The longer a cavity remains with infection, inadequate drainage, or foreign bodies the more fibrosis and the less likelihood of closure.

5. At times the tract leading to the focus is very long and passes near important structures or organs. In many of these cases it would not be advisable to follow the tract in operating. Lipiodol injection in determining the location of the focus allows a planned and more effective operative approach.

6. This work does not presume to add any new diagnostic features to the interpretation of the roentgenograms. It is hoped that the technical points in injection will be of value to anyone performing these studies.*

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* Since the preparation of this paper an article on the same subject has appeared in this Journal (Pendergrass, R. C., and Ward, W. C. Roentgenographic demonstration of sinuses and fistulae. Am. J. Roentgenol. & Rad. Therapy, 1947, *57*, 571–577).

PRINCIPLES OF FAST ELECTRON THERAPY IN CANCER*

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IN CONSIDERATION of the progress made during the past fifty years in the treatment of malignant diseases by means of radiant energy, it is justifiable to state that the physical and therapeutic possibilities in this field have neither been exhausted nor utilized to their fullest extent. The developments in nuclear physics are of too recent date to have gained great importance in their biological application. The work in this field is only in its incipient experimental stage.

One form of radiant energy has attracted our special interest for many years, namely, the production and use of free electrons in the treatment of cancer. This idea does not seem to be extraordinary or even original, when it is recalled that the biological effects of roentgen rays and radium are due to secondary electrons which are produced when roentgen rays pass through tissue. The advantage of using free electrons directly for therapeutic purposes is found in their physical characteristics. They are small particles of matter, which, after being freed from their source, have a limited pathway. For all practical considerations their range is determined by the power which generates the electrons and this is therefore relatively easy to calculate and to control. Also of importance is the fact that the highest concentration of energy in an electron beam is not at the source, as is the case in the more traditional forms of radiation, but rather at the end of the beam.

These characteristics should have caused electrons to be attractive for the treatment of malignant disease and, indeed, such efforts have been made for many years. The reason for not taking advantage of this form of radiant energy lies in technical difficulties which have made it heretofore impossible to build the powerful generators necessary to create free electrons of sufficient intensity.

The range of free electrons produced with voltages generally used in deep roentgen therapy would be limited to fractions of 1 mm. in depth. Such electron beams are, of course, of little therapeutic value. In order to derive benefits from this source of radiant energy, electron beams have to be produced with a range of at least 15 to 17 cm. in depth, which in turn require electric energy of many million volts.

This problem was approached in a practical way for the first time by Lange and Brasch who built an impulse generator with 1.7 and 2.4 million electron volts. Their work was followed by Trump, Van de Graaff and Cloud who constructed a high voltage generator and an acceleration tube of up to 3 million electron volts. Free electron beams produced with these powerful apparatus provided for a range of several millimeters and fostered the hope that, in pursuing the technical principles of construction, greater ranges might be achieved. The construction of machines of greater and greater voltages on these principles, for the production of free electron beams, however, became obviated by the development of the betatron by Kerst.

The betatron opened an entirely new technical approach to this problem, and promised the production of a free electron beam with sufficient range for actual use in the treatment of deep-seated malignancies.

The present limitations in the use of radiant energy from traditional sources are not due to the fact that roentgen rays or gamma rays of radium do not sufficiently destroy malignant cells, but rather that in doing so they also damage normal tissue.

* From the Tumor Clinic of Michael Reese Hospital. Presented at the Forty-eighth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 16–19, 1947.

The radiation effects from roentgen rays and gamma rays decrease with the square of the distance from the source, and the amount of radiation which can be safely administerated is generally limited by the tolerance of the skin. In order to apply lethal doses to malignant tumors within the body, different entrance fields are chosen for the rays, and thus crossfire the body tissue. Such radiation produces undesired and unnecessary effects on the tissue surrounding the tumor, and thus limits their use in the actual treatment of malignant disease.

In contrast, a free electron beam of sufficient energy can be directed and applied in such a manner that the concentration of energy is greatest in the tumor itself and not in the skin. Practically no radiation effects will take place beyond the stipulated depths and the energy concentration in the overlying tissue, through which the electrons must pass by necessity, will be smaller than in the tumor.

When the betatron was first developed by Kerst it was used as a machine to produce roentgen rays. Since the acceleration process for producing a free beam of electrons is the same as that for the production of roentgen rays, it was felt that this was an avenue of approach for solving the problem of utilizing electrons for cancer therapy. The work to be reported here was carried out by one of us (L. S. S.), with the close cooperation of Kerst, Almy and Lanzl. We were privileged to use the 20 million electron volt betatron originally built by Kerst and at present in the Department of Physics at the University of Illinois in Urbana. Construction alterations in the original machine were necessary to make it suitable for the liberation of a free electron beam.

The betatron works on the principle that a quantity of electrons from a tungsten filament is injected into a vacuum chamber between the poles of an alternating current electromagnet. A fraction of the injected electrons is captured in circular orbits. Here they receive energy from the increasing magnetic field, gaining about 70 electron volts per turn and making about 300,000 turns to reach full energy in the case of the 20 mev. machine. After reaching their required energy, the diameter of the electron orbit is expanded. If the goal is to produce roentgen rays, the electrons are caused to strike a platinum target. In order, however, to produce a free beam of electrons from the betatron it is necessary to have an unobstructed path. The target, therefore, was removed and the injector so placed that the electrons during expansion of the orbit may move out and reach the region near the edge of the magnetic field, where they start moving in spirals of large pitch. If nothing further were done, the electrons would continue spiraling, and would come out through the walls of the magnetic chamber and spread in all directions about the machine. However, if a magnetic shunt is placed at the beginning of the spiraling region, the magnetic field in this area is nearly zero. This makes it possible for the electrons to enter this region and move in nearly a straight line for a distance of 10 cm. They emerge in a field which is so weak as to receive only a slight magnetic deflection before they pass through the window of the vacuum chamber and escape entirely from the influence of the magnetic field.

Without going into details of the technical construction, it may be said that the described method of removing the electron beam works satisfactorily. After slight adjustments we were able to obtain a well collimated beam of electrons from the betatron. The most intense beam yet observed produced ionization effects in a Victoreen thimble chamber at a distance of 1 meter from the window equivalent to that produced by 100 roentgens per minute of roentgen rays. At 35 cm. from the window an equivalent of 1,500 r per minute with an 8 square cm. field was observed. It is expected that this intensity can be improved by a factor of 10 or 100.

The main part of the beam of electrons as it emerges from the window has a height

of about 2 mm. and width of about 6 mm. A cross sectional appearance of the beam shows a fanlike tail which is produced by electrons which are not completely captured by the magnetic shunt. This tail can be eliminated by permitting the beam to pass through an aluminum window with a thickness of 1/1000 of an inch.

The electron beam from the betatron suffers considerable scattering in the air beyond the window. A cross section at a distance of 10 cm. reveals that the beam no longer has its original sharp outline and that the edges have become diffused. At this distance, the height is about 6 mm. and the width 13 mm. At 35 cm., the beam is about 2 cm. high and 4 cm. wide, and at 1 meter the beam has a mean diameter of about 12 cm.

If, however, the beam after emerging from the doughnut is allowed to enter another evacuated space, the divergence can be limited and the beam will remain small and well defined.

The electron beam produced in the 20 mev. betatron does not produce sufficient ionization in air to be self luminous, but its path can be made visible by placing a fluorescent screen in the beam at a slight angle. The actual penetration of the electron beam was determined by sandwiching a sheet of film between two pieces of presdwood of density equal to that of water. The edge of the film was coincident with that of the presdwood blocks which face the beam and the plane of the film was approximately parallel to the beam. A beam produced with 13 mev. penetrates 6 cm. which is in agreement with the theoretical predictions. Based on our calculations, a 30 mev. beam would produce more than 14 cm. penetration and a 35 mev. beam, 17 cm. The actual depths reached are now being measured and it is expected that they will conform with the theoretical calculations. These figures indicate a constant change in ionization which continually increases from the surface to a point near the end of the range. Beyond this end, there is a sharp decrease to practically zero ionization. The exit dose of an electron beam from the betatron is extremely small, and when measured behind 10 cm. of presdwood was found to be about 1 per cent of that at the front surface.

Collimation of a beam of electrons is relatively simple. Lead, however, is not a satisfactory material for this purpose, because it produces a large yield of roentgen rays when struck by high energy electrons. As the efficiency of roentgen-ray production decreases rapidly with decreasing atomic number, material of low atomic number such as hydrocarbons are very suitable for collimation. Wood or plastics are probably the most economical and satisfactory.

In conclusion, this outline describes the production of an electron beam from the betatron. It was shown that this beam can be well collimated, is homogeneous in energy, and of sufficient intensity to reach deep-seated malignant diseases. Considerable experimental work, however, remains to be done before clinical application of the betatron in the treatment of malignant tumors can be safely recommended.

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DISCUSSION

DR. J. G. TRUMP, Cambridge, Mass. Dr. Uhlmann and Dr. Skaggs and also their associates at the University of Illinois, particularly Dr. Kerst, are to be commended for their pioneering investigation of the use of high energy electrons for the treatment of deep-seated tumors. The possibilities of cathode rays for therapy have been appreciated for many years, but were limited by the relatively low ranges in tissue which were then available. The betatron and various linear accelerators now under development offer for the first time a means of giving such particles sufficient range to reach deep-seated tumors. The ranges indicated by Dr. Skaggs agree closely with the maximum penetration of 1 cm. per 2 million volts which we observed some years ago with a Van de Graaff electrostatic accelerator.[1]

[1] Trump, J. G., Van de Graaff, R. J., and Cloud, R. W. Cathode rays for radiation therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *43*, 728–734.

It is well established that the biological effect of high energy electrons and roentgen rays should be closely similar for the same amount of absorbed energy. Both these radiations release within the volume of the absorber the same kind of low energy electron ionization which produces the biological effect. The attractiveness of cathode rays for therapy, as pointed out by Dr. Uhlmann, lies in the fact that for an individual electron the ionization density is a maximum at the end of its path. This would lead one to expect that a concentrated ionization dose could be delivered deep within the body with relatively little dosage sustained by the intervening tissue and no radiation dosage sustained beyond the maximum range of the particles.

This favorable characteristic of individual electrons, however, is considerably modified by scattering. When a parallel beam of electrons enters tissue, the electrons do not all proceed in an undeviated course, but are scattered sidewise with the result that the maximum ionization produced by the beam occurs in the first half of their range.

Fortunately, because of momentum considerations, it would be expected that electrons of 20 to 40 million volts would scatter less than electrons of a few million volts. This would have the effect of moving the region of maximum ionization somewhat closer to the maximum range for such electrons. Nevertheless, in bringing the region of maximum ionization to a tumor at 10 cm. depth, for example, cathode rays of over 40 million volts would probably be required. Such radiation would produce considerable ionization beyond the tumor and possibly at the exit skin. It will be interesting to have this distribution of ionization further investigated by the authors as they proceed with their work.

In this connection it is of interest to observe that corresponding and perhaps even more efficient localization of deep tumor doses can be accomplished by roentgen rays of suitable energy.[2] This slide shows the conventional three-portal cross-firing technique used on a cylindrical phantom using a 2 million volt roentgen-ray beam at a 1 meter distance. In this case the tumor dose is 60 per cent higher than the maximum dose sustained anywhere outside the tumor. The threshold erythema dose for such 2 million volt roentgen radiation is in excess of 4,000 roentgens when administered in daily doses of 300 r. The next slide shows the distribution of ionization in the same phantom produced by continuous crossfiring technique. The tumor dose is now several times higher than that sustained by nearby tissue and over five times greater than the skin dose.

In conclusion, it is evident that both high energy cathode rays in the 20 to 40 million volt range and supervoltage roentgen rays in the 2 and 3 million volt range are capable in principle of delivering high deep tumor doses with a minimum damage to surrounding healthy tissue. If the cathode-ray beam can be kept relatively free from accompanying low energy electrons, it is probable that unusually high skin tolerance will be observed at the portal of entry, similar to that found with supervoltage roentgen rays. The use of the high energy cathode rays for deep tumor irradiation is a new possibility in therapy, and its investigation deserves particular attention and support.

[2] Trump, J. G., Moster, C. R., and Cloud, R. W. Efficient deep tumor irradiation with roentgen rays of several million volts. AM. J. ROENTGENOL. & RAD. THERAPY, 1947, *57*, 703–710.

PART TIME RADIOLOGICAL PRACTICE IN HOSPITALS OF SMALL CITIES

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MANY communities of 10,000 to 25,000 population do not have a qualified full time radiologist.[1,2] It is doubtful if most of these communities now offer enough opportunity for advancement to attract one. In time, with a continued increase in the demand for radiology and completion of the proposed hospital building program, some of these smaller centers of population will support a radiologist. Most physicians who find it necessary to interpret roentgenograms for themselves are not well satisfied with the results of this practice. Hospitals which do not have specialists in radiology on their staffs are anxious to improve their roentgen-ray services. There is no lack of willingness on the part of most small hospitals to conform to the desirable standards[3,4] which have been recommended. Unfortunately, these standards, as far as obtaining qualified radiological consultation is concerned, are not easily met. In order to supply this consultation service,[5] physicians and hospitals in some of these communities are seeking part time visits from experienced radiologists located in neighboring large cities.

This discussion is presented to describe how one group of radiologists attempted to meet the demands for roentgen-ray service in outlying hospitals situated near a large city. This group is located in a city of 300,000 population situated in one of the more populous mid-western states. They maintain private offices and they also direct hospital roentgen-ray departments in their home city. In the beginning, the group was formed by a local radiologist inviting an out-of-town radiologist to join him in practice. Later, a third and then a fourth radiologist joined the group as the demands of the practice increased. Even before the war time shortage of radiologists became acute, this group had consented to make regular biweekly visits to conduct the roentgen-ray activities in three neighboring communities. This was arranged in addition to their office and hospital practice within the city limits. After Pearl Harbor, a hospital in another city was added for the duration of the war.

The first out-of-town venture by these radiologists was begun eight years ago at Hospital "A," an institution of 75 beds, serving a community of 25,000 population forty miles away from the city. No radiologist was available locally and the medical staff with the hospital authorities requested help in conducting the department of radiology. Within one year, a new hospital of 50 beds, Hospital "B," was opened in a community of 10,000 population fifteen miles from Hospital "A" and only forty-five miles from the city. A request was made by this hospital for visiting radiological service under the same plan. Because of their proximity it was possible to combine visits to Hospitals "A" and "B" on the same trip, thereby reducing the total travel time for each.

Six years ago Hospital "C," of 75 bed capacity located in a city of 15,000 population, asked for help with its radiological problems. This city is located thirty-five miles northwest of the home city, whereas Hospitals "A" and "B" lie to the east. When the radiologist who had practiced in this community died, the hospital purchased the apparatus which he had installed in it. Since there was no other radiologist in this community, the physicians and the hospital authorities requested the services of the group from the larger city. Adequate professional service to this hospital necessitated two visits each week totaling one to one and one-half days. To provide for this additional work load, it was necessary for the group to expand by the addition of a third radiologist.

Hospital "D," of 100 beds, located in a

25,000 population city was fourth applicant for consultation service. To meet its request, the radiological associates were required to extend by sixteen miles the eastern leg of their circuit. The distance to the east was now too great to be practicable except as a war time accommodation. It was undertaken only with the understanding that visits would be discontinued when the radiologist situated in the outlying city returned from military service. During the three and one-half years that this hospital was included, films were mailed once each week to the city office of the group. In addition, once each week, this hospital was visited by a group member as a part of the eastern trip which now required a minimum of twelve to fourteen hours, even under the most favorable travel conditions. Since the end of the war, our radiological service has been discontinued in Hospital "D" but continued in the original three hospitals.

In many localities, visits to three hospitals in one day, and a trip of one hundred thirty miles would not be possible. In this instance, the location of the hospitals in proximity, excellent roads which are seldom impassable in winter, and a level terrain, require that only a relatively small portion of the day be spent in transit.

These small city hospitals were founded by contributions from the local community and by large individual bequests. Their continued support comes from local citizens, community groups, church organizations, the hospital guild and occasionally from the municipal government. The board of directors of these hospitals usually include individuals or their representative who have contributed generously to the hospital, business men of the community and one or more physicians. The desire of all is to make the hospital in which they are interested as self sufficient and up to date as possible. In order to do so, the roentgen department as well as other divisions of the hospital must meet certain requirements. Hospital boards are usually well informed regarding the importance of professionally supervised roentgen-ray activities. By first-hand individual experience and through the advice of medical associates, board members are impressed with the fact that radiological services of high quality constitute an essential phase of hospital procedure. It is because administrative bodies look upon radiology as a primary hospital function that sharp differences in opinion have arisen with radiologists who seek to preserve strict private practice status in all their activities.

An experienced radiologist engaged in active private practice knows well the pitfalls which attend improper organization in the roentgen department of a hospital. Frequently, he can prevent dissatisfaction on the part of the board by explaining the function of the radiologist and by emphasizing his standing as a medical consultant.

The periodic visits of a consulting radiologist to outlying hospitals are necessarily limited in time. Organization of his time and efficient planning of all departmental activities is the secret of a pleasant and successful visit. Much of the technical work, outlined and directed in advance, should be completed before he arrives. Finished roentgenograms should be assembled and immediately available for his inspection. Pertinent information relative to the diagnostic examination should be collected by the technician in readiness for the radiologist. If the patients to be examined by him personally have been given a specific appointment for the occasion of his visit they can be handled without great time loss. The balance of the radiologist's visit is devoted to the very important function of professional consultation with his medical colleagues. The value of this last activity will depend upon the performance and ability of the radiologist as well as his personality.

In most instances, hospitals have been established long enough to acquire some roentgenologic equipment and develop floor space for the roentgen department before the trained radiologist is engaged. He must, therefore, put up with the physical plant which is available until he can plan and secure arrangements more to his

liking. There are certain physical requirements essential to the successful operation of any hospital roentgen department. These are determined by the number and type of patients in the hospital, the average length of hospital stay and the number and type of out-patients examined. If roentgen therapy is employed, adequate space for equipment, dressing rooms, examination facilities, and a waiting room for patients must be provided. Only those types of equipment which will be used frequently are justified. If an estimate of the number of fracture, gastrointestinal, urological and chest cases during one year is secured, a basis for equipment needs can be established. Special apparatus, as for example, that employed in examination of the skull is very useful but not essential in a small hospital.

A general hospital of 50 to 75 beds serving a community of 10,000 to 20,000 population needs as a minimum the following roentgenologic equipment: one combination fluoroscopic and roentgenographic tilting roentgen table, one fluoroscopic tube below and another roentgen tube above the table with energizing apparatus of 200 milliampere capacity. The added expense of a rotating anode tube seems justified if new equipment is to be purchased. One cassette changer and one mobile roentgen machine with about 30 milliampere and 85 kilovolt capacity are also needed. Usually the electrical circuits in the patients' rooms are inadequate for maximum operation, but special wiring should be available in the fracture room and the mobile apparatus used there whenever possible. Accurate and dependable temperature control for film processing solutions is a frank necessity; it is not a luxury. It is poor economy to permit laxity or inaccuracy in the processing of roentgen film which is a costly commodity, and upon whose roentgenographic quality, good clinical results depend. A generous stock of roentgen films in a light-proof film bin, adequate cassettes for any type of examination, a supply of film hangers for a half day's work, and a film dryer of two dozen film capacity are required. In the consultation room a bank of four viewing boxes and a stereoscope are required for proper demonstration and interpretation of films. Files for active films, the storage of inactive films, identification cards and diagnostic indexing of cases must be readily accessible. The personnel employed in the roentgen department should include a well trained and experienced technician, a relief technician who may spend part of her time in another part of the hospital and a part time stenographer who can take and transcribe medical dictation.

Planning in advance with the technician how the work is to be carried out in his absence will save much time for the radiologist during his subsequent visits. A list of all types of roentgen examinations ordinarily performed in the department, designating the various views to be made for each examination and the size and number of roentgen films required in each instance is advisable. This list, prepared by the radiologist, avoids leaving the choice of views to the technician or the referring physician and helps to prevent re-examination during the radiologist's visit because he finds filming inadequate or improperly performed. Patients referred for routine roentgen examination should not be scheduled during the radiologist's visit. Those for examination of the gastrointestinal tract may be scheduled according to either of two different routines. If the radiologist visits the hospital in the morning, the patient should receive his barium at the time he is fluoroscoped by the radiologist. If the visit does not occur before noon, the patient should be scheduled to appear four to five hours beforehand, given the barium meal and films made of the stomach and duodenum. This method of procedure gives the radiologist a preview of the stomach and duodenum, permits observation of the rate of movement in the upper gastrointestinal tract at the time of his fluoroscopy, de-

creases the amount of subsequent filming and avoids further delay before the patient can be fed.

Direct roentgenological consultation in emergency situations is not available in a hospital served by a visiting radiologist unless such situations arise during or shortly before the specified time of his visit. Actually, this shortcoming is less important than many persons are apt to believe, because few roentgen examinations fall in the true emergency category. A firm stand by the radiologist in the matter of postponing the roentgen examination of patients with severe injuries, such as skull fractures, until the more important treatment for shock has been instituted, is sound medically and results in less hurried and therefore more accurate and informative roentgenograms. Most physicians in outlying hospitals have been in the habit of treating fractures without the help of a radiologist or of a traumatic surgeon. In the case of difficult fractures it is frequently necessary to call a specialist from a larger center or to send the patient to him for treatment. In the meantime, films can be sent to the radiologist or he will see them during the next scheduled visit. Probably the greatest value of the radiologist to the general practitioner in the management of fractures comes from discussions regarding further procedures, when the immediate attempts at reduction have not been entirely satisfactory. A radiologist who is consulting daily with orthopedists and traumatic surgeons of a large community acquires a fund of knowledge about fracture work which will make his judgment and advice of considerable value. Frequently the practitioner with a severe fracture case is undecided whether or not he should seek expert consultation. The radiologist may tactfully suggest, through an explanation of the points involved as shown by the roentgenographic examination, what may be the most advantageous procedure for the patient and physician. In a consulting practice of this type it is seldom necessary for the radiologist to provide fluoroscopic assistance during the reduction of fractures. Staff physicians should use the fluoroscope for such purposes only under the control of the technician, to insure due regard for the safety of examiner and patient. The upper limit of fluoroscopic exposure must be stated specifically by the radiologist, and the technician must have authority to discontinue the roentgen ray if this amount is exceeded.

During the interpretation of roentgenograms much interesting material passes before the radiologist. It is our practice to classify all cases at this time according to diagnosis. For this procedure the simple and very workable system devised by Hodges and Lampe[6] is used in these hospitals. Standardization in all activities of the group in the matter of record keeping has served to coordinate the clinical experiences at all hospitals as well as the private office practice.

Administration of roentgen therapy on a consulting visit basis presents a very difficult problem. Certainly from the viewpoint of the group radiologist the simplest and most satisfactory course to follow is to require that all ambulatory patients travel to his established office and have bed-ridden patients transferred to hospitals served by the group in the home city. From the viewpoint of the patient and in the eyes of the management and medical staff of the small city hospital this is scarcely to be considered ideal.

Difficulties in securing daily transportation of patients to the city for a number of successive weeks is an insurmountable obstacle in some cases. Many patients from outlying districts will not forego the association with their family and friends resulting from confinement in a hospital away from home. They will, however, go to the local hospital in which they have confidence and where they believe they will be more comfortable. Local pride of hospital authorities, citizens and the medical staff in their institution urges that the patients

from their community be kept at home. Without knowing or weighing the factors involved many persons influential in the hospital feel their institution should be able to give roentgen therapy as satisfactorily as those in large cities.

Before the group became interested in the out-of-town hospitals, two of these institutions had acquired roentgen therapy apparatus. When the radiologists of the group were asked to direct the departments in the hospitals the question of roentgen therapy presented a real challenge. As a result the radiologists decided to determine if a workable procedure for roentgen therapy could be devised, primarily for patients who could not be treated in the city, in place of giving a dogmatic "no" to consideration of any therapy.

In this plan the technician must be especially well trained in roentgen therapy. Adequate equipment of not less than 200 kilovolt capacity must be provided, as well as proper facilities for examination of the patients. Each patient receives a preliminary examination by the radiologist after referral from his physician. If it appears that he should not be treated in the local hospital and can be transferred to the city for more adequate therapy, the radiologist makes this recommendation to the referring physician. The radiologist must always reserve the right to determine where the patient should be treated. If the patient is to be treated in the local hospital, the history and the radiologist's physical findings are recorded on the treatment record. Specific written instructions regarding dosage and positioning are also recorded. The patient is then given his first treatment by the radiologist with the assistance of the technician. All the subsequent treatments given on the days that the radiologist is present are performed under his immediate supervision. He must also review the treatment record on each of these visits and write instructions for any interim treatment before the next biweekly visit. A responsible physician who has had some postgraduate training in radiology should be employed to supervise and check the technician's treatment in the absence of the radiologist. Because of the radiologist's responsibility, it is advisable for him to inform the patient, before treatment is started, that he will not be present during each treatment. He should tell the patient what arrangements have been made for supervision. If the patient does not wish to take treatment under these conditions he may refuse and the radiologist must return him to his referring physician with the explanation for his action. The biweekly examination of the patient will keep the radiologist informed regarding the development of untoward symptoms and the progress of the lesion. The experienced radiologist who carefully observes his cases should know beforehand when to terminate treatment and avoid either under or excessive dosage.

Roentgen therapy of superficial lesions may be performed if suitable apparatus is available. Treatment of this type is confined strictly to the time of the radiologist's visit and administered under his personal supervision.

The record system should be similar to the one used in the city. Patients for follow-up examination are scheduled weeks or months ahead on the day and hour of the radiologist's visit, and as careful a reexamination conducted as is employed elsewhere. It is the practice to see all such patients from the community during his visits in the local hospital whether they were treated locally or in the city. This encourages more patients to return for post-treatment examinations.

If radiation therapy is administered with a full realization of these limitations and an energetic interest on the part of the radiologist is maintained, the procedure as outlined seems justified.

Intracavitary radium application can be performed by the radiologist on his visit to the hospital, if it is his practice to do this type of work. Patients so treated usu-

ally receive roentgen therapy in his home office or the hospital, thereby allowing him to plan the proper sequence of treatment. The nursing personnel of the hospitals quickly become accustomed to the routine care of patients treated with radium. Specific and clearly stated directions covering all phases of the patient's care, and instructions concerning telephone communication with the radiologist are the same as used in the city hospitals. These have been found entirely satisfactory for the protecting of the patient as well as for the hospital personnel. If no one in the radiological group is equipped to apply radium, it is apt to be administered by those untrained in such procedures, obviously making the results of radiation therapy less satisfactory. All patients who receive radium application are considered the radiologist's private patients.

A recent survey of the departmental records shows that the number of diagnostic roentgenologic cases per year increased 100 to 150 per cent between 1940 and 1946 in all of the out-of-town hospitals. The major increase in Hospital "A" occurred in 1946 after many physicians returned from service. Hospitals "B" and "C" showed their major increases during the war, when large industrial plants were built in the communities. The increases in these hospitals have been maintained since the war and augmented by patients referred from many returned physicians. A continuation of the present level of activities in each radiological department depends upon the financial status of the local community, new hospital construction, and the use of roentgen equipment in the offices of staff physicians. The quality of the service rendered by the visiting radiologist will do much to offset the latter and also maintain present activities.

The most important consideration in discussing remuneration is the assurance that the radiologist will find he is sufficiently well paid to maintain the active interest, which is essential to successful medical performance. If the radiologist does not enjoy his out-of-town visits, no reasonable remuneration can compensate him. On the other hand, if a break in the routine of city practice can be accomplished, without disrupting the continuity of service, as is possible where a group of radiologists is practicing together, these trips may be a welcome diversion. Scheduling hospital visits during time ordinarily devoted to recreational activities, as week-ends or "half days," is not recommended. Such a practice may exact a price out of all proportion to any remuneration received.

Hospitals of less than 50 bed capacity may not have enough roentgen-ray work to pay a radiologist on a percentage basis. In this event, he may receive a fixed sum for each visit. The minimum number of visits per week or per month should be stipulated. With a larger volume of roentgen-ray work, a percentage of the gross income should be received. Remuneration in proportion to the work performed is a definite incentive to his development of the roentgen department. In calculating the radiologist's income, his extra expenditure of time and effort in travel is balanced, at least in part, by the fact that he is not in the hospital for more than a short period during each week.

Charges for roentgen examinations must be determined by the radiologist, and with the agreement of the hospital authorities. They should be in accord with charges for similar service in the locality. Fees for roentgen therapy are determined entirely by the radiologist, after his examination of the patient and outline of necessary treatment. In these out-of-town hospitals, the character of the visits makes it necessary for the hospital to collect the roentgen-ray accounts. Settlement of the radiologist's account at the end of each month is recommended. In order to do this, the amount represented by the current bad debt loss ratio of the hospital may be deducted, in determining the gross income. This avoids endless bookkeeping and permits the radi-

ologist's account to be kept in balance. When the bad debt loss ratio is not determined, the radiologist should receive a percentage of the monthly gross charges. This should be slightly less than the percentage received in the plan previously mentioned. Kirklin,[7] Ullmann,[8] Sante,[9] and Warfield[10] have stated their ideas concerning methods of remuneration. Considering all factors, it appears that the figure of 40 to 60 per cent of gross receipts, or its equivalent, as recommended by Kirklin,[7] is fair if the hospital has a reasonable volume of work and the radiologist's loss because of absence from his city practice is not large.

SUMMARY

(1) The experiences of a group of radiologists in conducting a consultation practice in small out-of-town hospitals is described.

(2) Suggestions for operating a diagnostic roentgenological service are given and necessary equipment listed.

(3) Administration of radiation therapy is not advised in these hospitals except as specified.

(4) The development of departmental activities under the guidance of a qualified radiologist is reported.

(5) Factors determining the radiologist's remuneration are discussed.

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DEPARTMENT OF TECHNIQUE

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CONTRIBUTION TO THE TECHNIQUE OF BRONCHOGRAPHY IN ADULTS*

By L. WALK

THE introduction of a rubber tube into the trachea, for bronchography, is apparently considered to be technically difficult, and this even seems to inhibit a wider use of bronchography. In this article a simple method is described.

The patient is sitting, leaning about 10 degrees forward. A duodenal tube is held between the second and third fingers of the left hand (Fig. 1); these two fingers with the tube are introduced into the pharynx, behind the epiglottis which can be easily palpated, and the epiglottis together with the tongue is pulled forward somewhat. The tube is thus held against the posterior surface of the epiglottis. The patient is asked to breathe deeply. *During every deep inspiration* the free right hand pushes the tube 1 or 2 cm. forward; the fingers of the left hand holding the tube are somewhat loosened for this. When the tube has entered the trachea, it is felt falling loosely (contrary to the tight going if erroneously introduced into the esophagus). If the first attempt is not successful, the next is made with the patient leaning a little more forward (up to 45 degrees). The introduction is performed without light, the roentgenologist thus adapting his eyes for the following roentgenoscopy. The iodized oil is instilled under roentgenoscopic control; diagnostically valuable aspects and moments are fixed by means of fluoroscopic spot films.

Before the introduction of the tube the patient has to fast and is prepared as follows: Half an hour before the exploration morphine (or best dihydrocodeinone) plus atropine is injected. Then the throat is anesthetized by means of soft cotton brushes; first the pharyngeal arches, the upper and then the lower part of the piriform recesses are anesthetized (e.g. pantocaine 2 per cent, to which 1 to 2 drops of adrenaline per cc. have been added), the anesthetic spreading over the pharyngeal mucosa even where not touched by the brush. Usually three to four brushes are sufficient. An introduction of a brush into the trachea is not necessary and only means discomfort to the patient. An inspection of the larynx by means of a mirror follows, looking for vocal cord paresis. Then 2 cc. of the anesthetic is injected into the trachea by means of a laryngeal syringe, which is held at the posterior surface of the epiglottis and is not introduced into the trachea; the injection (under mirror

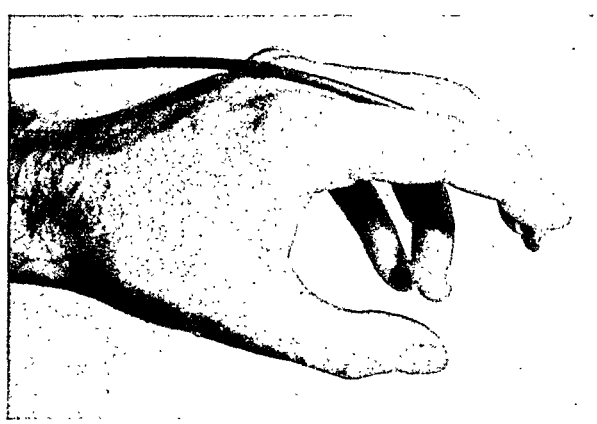


Fig. 1. Duodenal tube held by the second and third fingers of the left hand, for introduction. A tube with a small metal olive is used.

* From the I. Medical Clinic of the University of Tartu.

control) is done promptly during the inspiratory phase of deep breathing and causes expectoration. A spray may be used for anesthesia instead of the first brushes.

The duodenal tube can be introduced without dyspnea and insults of expectoration even in unilateral vocal cord paralysis.

SUMMARY

A description has been given of a simple method for introducing a duodenal tube into the trachea for bronchography.

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MALLEABLE CONES FOR ROENTGEN THERAPY*

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THE use of small cones for direct treatment of limited areas has become universally adopted in recent years, particularly for lesions in various accessible body cavities. Because large doses may be applied directly to the tumor and because accurate control of the treated areas is possible with intracavitary cones, results in many cases have been very gratifying.

One difficulty that plagues the radiotherapist in the application of this type of treatment is his all too frequent inability to adapt a rigid cylinder to lesions whose dimensions do not approximate a circle. The smallest cylinder that will cover the lesion frequently does not leave sufficient margin of apparently uninvolved tissue to take care of invisible extensions, while a cylinder large enough for the greatest diameter of the lesion will necessitate treating an unjustifiably large amount of normal tissue. Various limiting diaphragms on the ends of the cones have been tried, but are difficult to adjust properly. Another objection to the use of large cylinders in this work is that frequently sufficient space is not available.

An attempt to overcome at least part of these difficulties has been made by the use of "malleable" or "moldable" cones. These were made in the following sizes, 2.5×40 cm., 3.5×40 cm., and 5×50 cm. They are constructed of 1/16 inch lead sheet rolled into cylinders and fitted with hubs to fit the cone carrier of the machine. With simple tools or strong hands the apertures may be changed so that they are adapted to the treatment of a large variety of lesions. The original models were made with soldered seams. This gives some difficulty in molding which would be obviated if seamless lead tubing were used.

In practice, the ends of the cones are coated with paraffin or encased in a thin rubber sheath, since the bare lead is rather unpleasant to use.

To date these accessories have been successfully used in the treatment of carcinoma of the tongue, tonsil, buccal mucosa, alveolar process and palate. The 5 cm. size has also been used for external irradiation in the submental and submaxillary areas to which it may be shaped so that large doses may be given with good protection for the mandible.

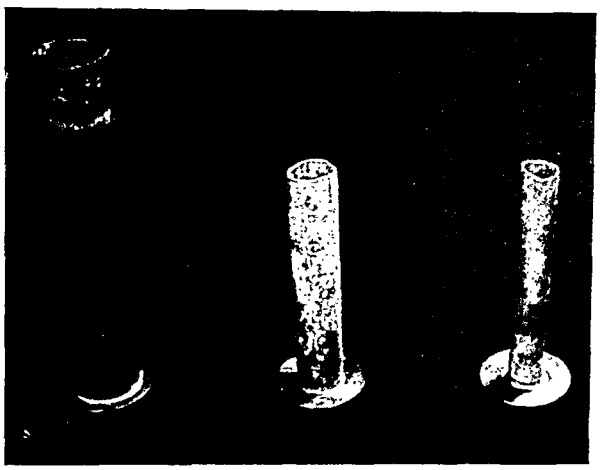


FIG. 1.

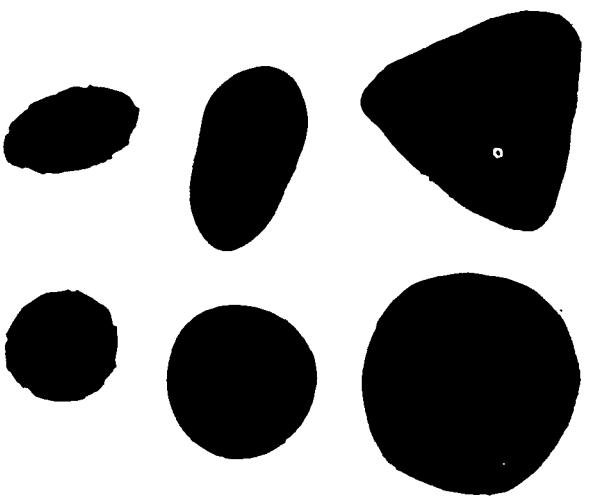


FIG. 2.

* From the Department of Radiology and Physical Medicine, University of Minnesota, Minneapolis, Minnesota.
† Trainee of the National Cancer Institute.

Figure 1 shows the original group of cones made at the University of Minnesota. Figure 2 is a reproduction of a film exposed with the cones molded in various shapes. The original film showed an even grayness over the treatment area indicating a satisfactory uniformity of field.

University Hospital
Minneapolis 14, Minn.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Fiftieth Annual Meeting: Netherland Plaza Hotel, Cincinnati, Ohio, October 4–7, 1949.

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Thirty-first Annual Meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

EDITORIALS

LEGG-PERTHES' DISEASE

THE literature of Legg-Perthes' disease is voluminous. Since first recognized by Legg and Waldenström, later followed by Calvé and Perthes, the literature is replete with articles in which the disease is discussed from all standpoints. The observations of the earlier writers have been proved to be well founded except for the etiology which remains obscure. From the study of pathological specimens, it is now generally accepted that the primary process is an aseptic necrosis, followed by resorption of necrotic cancellous tissue and, last, formation of new bone and cartilage. Among the names given to the condition, none is entirely satisfactory. Perthes' suggestion of osteochondritis deformans is not apt as it suggests an inflammatory process, which it is not. It is neither an osteitis nor a chondritis. Coxa plana is used by some authors to designate a late untreated aspect of the disease, although Waldenström emphasizes the fact that flattening may occur early in its course. Osteochondrosis is becoming a more acceptable term.

The similarity of Legg-Perthes' disease to foci of aseptic necrotic changes in other epiphyses has been noted and it is now generally accepted that the condition in the hip joint is analogous, in fact similar to those found in other epiphyses. Circulatory disturbance is regarded as the exciting cause of the necrosis. Coincidentally reports have appeared of other conditions which can simulate the appearance of Legg-Perthes' disease, such as hypothyroidism, Gaucher's disease, the end results of reduced congenital dislocation of the hip, and possibly, the changes seen in caisson disease which may resemble a late untreated end result of osteochondrosis of the hip.

That Gaucher's disease can produce a similar picture has been described previous to the present time[1] (Reiss and Kato,[2] 1932, Schein and Arkin,[3,4] 1942, 1948). In these papers, the literature of skeletal changes of Gaucher's disease has been reviewed and other earlier instances are given. Arkin and Schein suggest that the Gaucher cells, which are known to surround and infiltrate small arteries and capillaries, at times do so in a fashion sufficient to cut off circulation and to produce aseptic necrosis of bone. In 1938, Albright[5] reported a case of myxedema with changes in the hip joint simulating those found in Legg-Perthes' disease. He quoted Looser who found that the pathological change in hypothyroidism was retardation in the transformation of cartilage to bone in the epiphysis. Wilkins[6] (1941) reported additional cases. He stated: "I wish to stress, however, that true epiphysial dysgenesis can be differentiated with certainty from other conditions which might simulate it in a single roentgenogram only by following the stages of ossification in serial roentgenograms."

Our conceptions of disease entities undergo frequent changes as our knowledge of a disease process progresses. Much depends

[1] Draznin, S. Z., and Singer, K. Legg-Perthes' disease: A syndrome of many etiologies? With clinical and roentgenographic findings in a case of Gaucher's disease. AM. J. ROENTGENOL. & RAD. THERAPY, October, 1948, *60*, 490–497.

[2] Reiss, O., and Kato, K. Gaucher's disease; clinical study, with special reference to the roentgenography of bones. *Am. J. Dis. Child.*, 1932, *43*, 365–386.

[3] Schein, A. J., and Arkin, A. M. Hip-joint involvement in Gaucher's disease. *J. Bone & Joint Surg.*, 1942, *24*, 396–410.

[4] Arkin, A. M., and Schein, A. J. Aseptic necrosis in Gaucher's disease. *J. Bone & Joint Surg.*, 1948, *30-A*, 631–641.

[5] Albright, F. Changes simulating Legg-Perthes disease (osteochondritis deformans juvenilis) due to juvenile myxoedema. *J. Bone & Joint Surg.*, 1938, *20*, 764–769.

[6] Wilkins, L. Epiphysial dysgenesis associated with hypothyroidism. *Am. J. Dis. Child.*, 1941, *61*, 13–34.

upon individual definition of a syndrome or a disease entity. The roentgen picture alone does not constitute sufficient evidence to consider a certain condition as a syndrome or disease entity unless it be labeled a roentgen syndrome or entity. The clinical, pathological and etiological features must also be taken into consideration. Thus, in the case of Legg-Perthes' disease the clinical history, the physical signs and symptoms have often been described and a fairly constant clinical picture has resulted. These taken with the usual roentgen findings may be said to be an entity.

It can be assumed that no roentgenologist will make a final diagnosis without a knowledge of the clinical history, physical examination and pathological data of the patient. It is without doubt of value to present articles in medical journals calling attention to the fact that Legg-Perthes' disease, for instance, may resemble in its roentgenographic findings, Gaucher's disease, hypothyroidism and other conditions, so that the similarity may not be overlooked or forgotten. But, to state that Legg-Perthes' disease is not a clinical entity may lay too much stress on the fact that only in its roentgen manifestations is it simulated by those of Gaucher's disease and other conditions. This may lead young and enthusiastic roentgenologists to suggest that every case is due to hypothyroidism, Gaucher's disease or to an old reduced congenital dislocation of the hip, and so forth, ignoring the clinical findings. This would not redound to the roentgenologist's reputation for diagnostic acumen. When the roentgen findings and the clinical history, physical signs and symptoms are those of Legg-Perthes' disease the diagnosis, therefore, is a sufficiently satisfactory one.

Ralph S. Bromer, M.D.

HIRSCHSPRUNG'S DISEASE

NUMEROUS articles on megacolon had appeared in the literature prior to Hirschsprung's first report in 1888. In this report he described two cases with symptoms of constipation and meteorism and without evidence of stenosis of the colon. Later, Hirschsprung reported additional cases and he attributed the cause of the dilatation to a congenital defect, and since his report Hirschsprung's name has been attached to that type of congenital dilatation of the colon which occurs in children.[1]

During the following years since Hirschsprung's original report many attempts have been made to ascertain the exact pathogenesis of that disease and to devise satisfactory treatment, but it has only been within the last few years that real progress has been made.

Ehrenpreis[2] in 1946 produced evidence that the dilatation of the colon is not congenital, but develops weeks or months after birth and he, along with many others, classified megacolon as a dysfunction of evacuation of unknown origin. A disturbance of autonomic innervation of the colon seemed to him most probable but not proved as neurohistological investigations had given contradictory results.

In 1948 Swenson and Bill[3] reported that suitable methods of roentgenological examination reveal a "spastic" segment of colon distal to the dilated part and they concluded on clinical grounds that this obstructive narrowing is responsible for the dilatation.

Quite recently Bodian, Stephens and Ward[4] at the Hospital for Sick Children, London, England, have reported on their study of Hirschsprung's disease and idiopathic megacolon in which they employed the roentgen ray as a method of differentiation. They employed no routine preparation prior to the administration of the barium and in order to avoid the sequelae of desiccated barium in the colon, glycerine and paraffin were introduced into the barium emulsion. This was run into the bowel from an initial height of 3 feet above the table through a soft rubber catheter introduced a minimum distance into the rectum. The flow was under the immediate control of the roentgenologist and the initial filling of the rectum and rectosigmoid region was closely observed. The flow of the enema was stopped as soon as the diagnosis could be made, the flow of the enema being stopped at various stages of filling of the colon, and posteroanterior, lateral and oblique views taken in such positions as would best show the abnormalities and the rectosigmoid region. Roentgenograms were also taken immediately after evacuation.

The roentgen findings were characteristic of Hirschsprung's disease in 34 of their cases. In the chronic stage of the disease the plain film of the abdomen may show gross gaseous distention with the flaring of the ribs and the distended colon immediately below the diaphragm on both sides. During the barium enema study the rectum is filled and this appears to be normal or less than normal size. Above the rectum the diameter of the intestine narrows for a short distance which varies greatly from case to case. Above this narrowed portion the colon opens by a wide funnel into a hugely dilated and gas-filled colon. Once this dilated portion is filled, the narrowing below or distal to it may be obscured and very difficult to demonstrate. Consequently it is important that not too much barium be given so that it obscures the narrowed segment proximal to the normal rectum. It is necessary that the examiner watch with considerable care the filling of the rectum and the rectosigmoid area to observe not only the narrowed loop but to vary the position of the patient so that film studies may be made at the exact

[1] Bockus, Henry L. Gastro-enterology. Vol. II. W. B. Saunders Co., Philadelphia, 1943, p. 398.
[2] Ehrenpreis. Quoted by Bodian, Stephens and Ward.[4]
[3] Swenson and Bill. Quoted by Bodian, Stephens and Ward.[4]
[4] Bodian, M., Stephens, F. D., and Ward, B. C. H. Hirschsprung's disease and idiopathic megacolon. *Lancet*, Jan. 1, 1949, *1*, 6–11.

interval of the filling of the narrowed loop and the beginning filling of the funnel-shaped colon above it, as it is this narrowed segment of the colon in the rectosigmoid area which gives the clue in the differential diagnosis between Hirschsprung's disease and idiopathic megacolon.

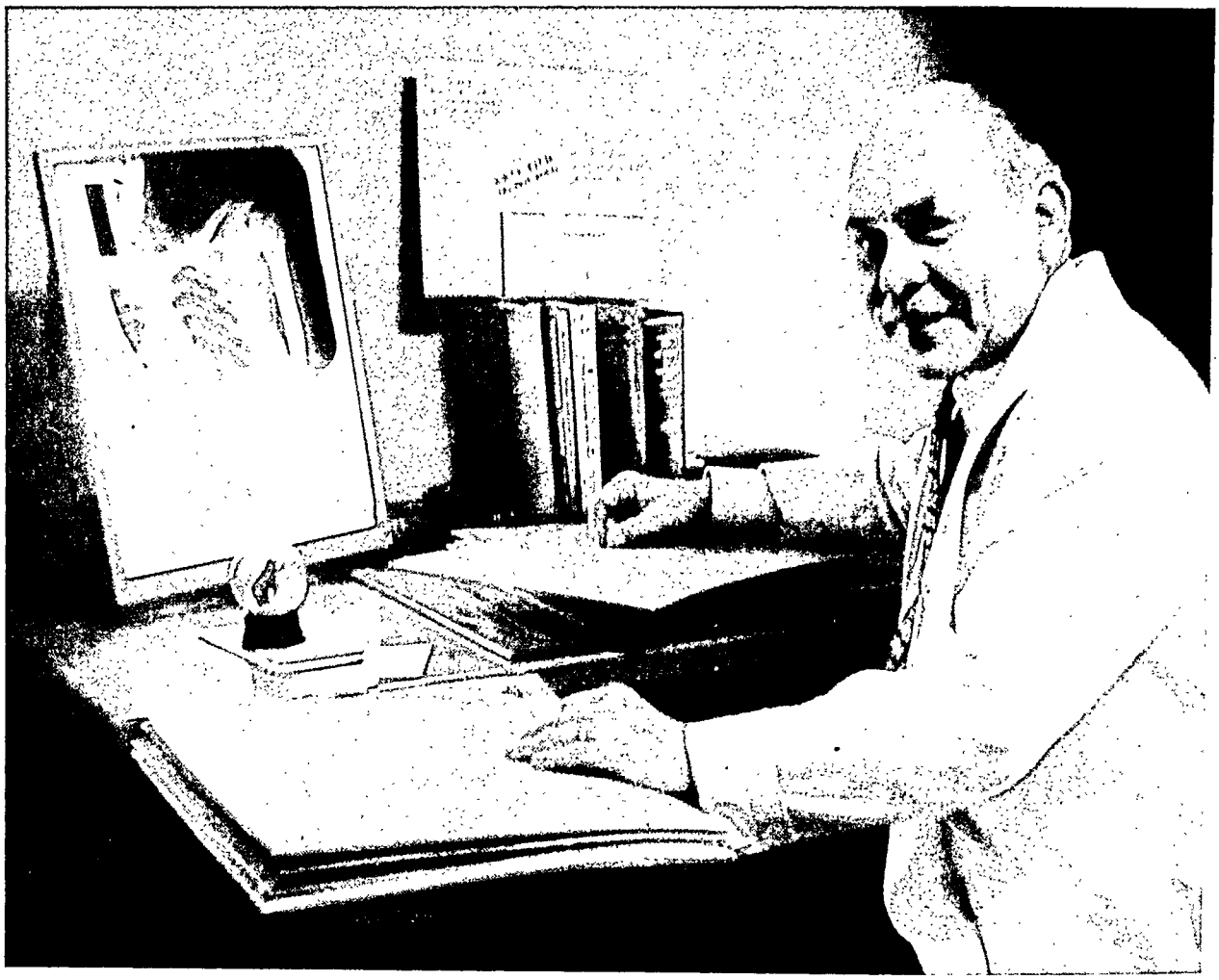
The cases of idiopathic megacolon in the study by Bodian, Stephens and Ward fell roughly into two subgroups: One group in which the distention was confined to the rectum and the distal pelvic colon forming a terminal reservoir, and a second group in which there was noted tubular dilatation which extended from the anal orifice throughout the colon. In those cases of idiopathic megacolon in which there is a terminal reservoir present, a preliminary film of the abdomen may show a portion of dilated gas-filled intestine and the barium enema reveals that the rectum and the distal pelvic colon form a pear-shaped unilocular dilated chamber extending in some cases from the anus to the xiphisternum.

In those cases which fall into the group classified as tubular dilatation, the rectum appears quite large and the pelvic colon is much longer and wider than usual and lacks its normal haustral markings, but the contour of the bowel is otherwise normal. The boundary between the normal and abnormal bowel is in this type of case ill defined.

The cause of the spasticity which is observed in the distal colon in Hirschsprung's disease was suggested by Zuelzer and Wilson[5] in their paper on "Functional intestinal obstruction on a congenital neurogenic basis in infancy" in which they reported several cases showing segmental aplasia of ganglion cells of the myenteric plexus in several infants with acute intestinal obstruction, but their findings in chronic megacolon were not uniform. Bodian and his colleagues attributed some of the discrepant findings of previous investigators to the assumption that all cases of idiopathic megacolon are Hirschsprung's disease. This group of investigators reserve the term Hirschsprung's disease for the condition in which a contracted segment of the bowel can be demonstrated roentgenologically, and in all the cases of this kind that they have examined histologically they have found complete aplasia of parasympathetic ganglion cells in the autonomic plexuses of the distal segment. Utilizing Swenson and Bill's principle of treatment by rectosigmoidectomy, they have had gratifying results in their group of cases.

The roentgenologist who so frequently sees these cases of dilatation of the colon may by careful examination definitely differentiate Hirschsprung's disease from the group of idiopathic megacolon by demonstrating the narrowed segment of the bowel in the rectosigmoid area in contrast to the idiopathic megacolon group which exhibits the terminal reservoir and the tubular dilatation of the colon. It is only by such a careful examination that true Hirschsprung's disease may be differentiated and by proper operative procedures, as suggested by Swenson and Bill, the condition relieved.

[5] Zuelzer, W. W., and Wilson, J. L. Functional intestinal obstruction on a congenital neurogenic basis in infancy. *Am. J. Dis. Child.*, 1948, *75*, 40–64.



WILLIAM GREGORY COLE
1902-1948

DR. WILLIAM GREGORY COLE died suddenly of coronary disease on April 15, 1948, while in Bermuda for a brief rest. Dr. Cole, the son of Dr. and Mrs. Lewis Gregory Cole, was born in New York City on February 1, 1902. He received his early education at Hackley School in Tarrytown, New York. He obtained his B.S. from Harvard University in 1924, and in 1928 his medical degree from the College of Physicians and Surgeons, Columbia University, and served his internship for two years. At the end of this period he entered the field of radiology under the guidance of his eminent father, Dr. Lewis Gregory Cole. They found each other stimulating collaborators. Dr. Lewis Gregory Cole tells in his recently published book "Lung Dust Lesions Versus Tuberculosis" of his son's part in interesting him in research on the effect of dust on the lung. He tells of William Gregory's putting a portable roentgen-ray machine in the back of his car and driving down to West Virginia; of his overcoming the suspicion and even animosity of the silicosis victims, and of his obtaining roentgenograms and pathological specimens, which were the basis of the elder Cole's researches in the pathology of these lesions. "Dry as dust" is an outmoded simile in any discussion of the studies of the Coles on pneumoconiosis. There is

dust, but there is also a rich storehouse of human relationships between doctors and patients, and father and son.

Dr. Cole went to Pittsfield, Massachusetts, in November, 1941, as roentgenologist to the House of Mercy Hospital where he served in that capacity until his death. He was also roentgenologist at the Hillcrest Hospital in Pittsfield and the Fairview Hospital in Great Barrington. He was a member of the Massachusetts Medical Society and had been certified by the American Board of Radiology. His application for membership in the American Roentgen Ray Society was pending at the time of his death and he was elected posthumously at the meeting of the Society in September, 1948.

During the few short years he was in Pittsfield, Dr. Cole made many true friends in the profession who will miss his keen wisdom and advice, not only in his chosen field of radiology but in various other fields pertaining to the practice of medicine. The new and modern Department of Radiology at the House of Mercy Hospital will stand as a memorial to Dr. Cole who planned and worked diligently to bring about its establishment.

Ramsay Spillman, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

AMERICAN RADIUM SOCIETY
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1949, to be announced.

AMERICAN COLLEGE OF RADIOLOGY
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: Atlantic City, N. J., June 8–10, 1949.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Next meeting time and place of Alabama State Medical Association.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. A. H. Levy, 1354 Carroll St., Brooklyn 13, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. George L. Sackett, 10515 Carnegie Ave. Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday of October and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

HOUSTON X-RAY CLUB
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA X-RAY CLUB
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

LOUISVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

Nebraska Radiological Society
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

Northern California Radiological Club
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August. Next meeting Sept. 27, 1948.

Ohio State Radiological Society
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Queens Roentgen Ray Society
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Robert M. Lowman, Grace-New Haven Community Hospital, New Haven 11. Meets bimonthly second Thursday, at place selected by Secretary.

Radiological Section, District of Columbia Medical Society
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of New Jersey
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Ralph E. Alexander, 101 Medical Arts Bldg. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Denver, Colo., August 18, 19, 20, 1949.

St. Louis Society of Radiologists
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

Section on Radiology, California Medical Association
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting Jan. 7–8, 1949, Fort Worth, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. Ivan J. Miller, 49 Fourth St., San Francisco 3. Meets monthly on third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Langley Porter Clinic, University of California Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Roentgen Society
Medical Members' meeting held monthly on third Friday at 2:30 p.m. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 2100 Marlowe Ave., Montreal 28, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 p.m.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

THIRD INTER-AMERICAN CONGRESS OF RADIOLOGY

The Third Inter-American Congress of Radiology will be held November 11 to 17, 1949, in Santiago and in Vina del Mar, Chile. The inscription fee of twenty dollars should be sent to Dr. James T. Case, 55 East Washington St., Chicago 2, Illinois. More than one hundred American radiologists have expressed their desire to attend the meeting and are investigating expenses, travel itineraries, reservations, etc. Information concerning these matters will be sent on application. Whether or not those who inscribe as members actually attend the Congress, they will be listed as members and receive a copy of the Proceedings of the Congress. Arrangements are in process for the United States participating in the program. Official topics for discussion, as previously published, are as follows:

A. Radiological Exploration of the Cardiovascular System with Opaque Material.

The official presentation should refer essentially to radiological exploration of the heart and large blood vessels. Inclusion in the official presentation of the peripheral vascular system will be optional.

B. Diagnosis and Simple Radiological Exploration of the Skull.

With the object of facilitating its development, this subject has been divided into three official presentations:

1. a) Skull in general.
 b) Sella turcica.
2. c) Orbits.
 d) Paranasal cavities.
3. e) Temporal bones.

These official presentations should be short communications, read without introducing individual cases, being a résumé of the experience of the country of the speaker. Official speakers may bring all the material they wish; preferably full-size originals for exhibition in the Scientific Exhibits. The Executive Committee requests that collaborations be fundamentally objective, and insists upon the exhibit, making the verbal part as brief as possible.

C. Radiation Treatment of Cancer of the Tongue.

D. Radiation Treatment of Cancer of the Cervix.

Official presentations on these two subjects should comprise essentially the following parts:

1. Radiotherapy Technique.
2. Immediate and Subsequent Reactions, and
3. Case Reports Illustrating Clinical Degree and the Histological Type of Cancer.

In addition there will be opportunity for so-called "free papers." These papers are to be presented in the Section on Scientific Exhibits.

Facilities are being provided for earphones so that those in attendance will be able to hear a paper read in the language in which it is being spoken or a simultaneously read translation. Our Chilean colleagues have pledged themselves to perform a tremendous amount of work to make the Congress proceedings available to all listeners.

Those who definitely decide to attend the meeting should communicate with the undersigned to receive complete instructions as to the necessary documents, such as passports, visas, health certificates, etc. Further information will be published as it becomes available. At the moment it is urged that all who wish to participate in the program let us know as early as possible.

James T. Case, M.D.
Regional Secretary
for the United States

SIXTH INTERNATIONAL CONGRESS OF RADIOLOGY

The Sixth International Congress of Radiology will be held in London from July 23 to 30, 1950, with Congress headquarters at the Central Hall, Westminster. The address of the Central Office is: 45 Lincoln's Inn Fields, London, W.C. 2. The Officers of the Congress are:

President—Dr. Ralston Paterson.

President Emeritus—Dr. A. E. Barclay.

Vice-Presidents—Dr. S. Cochrane Shanks, Prof. B. W. Windeyer, Prof. W. V. Mayneord, Dr. F. Gordon Spear.

Treasurer—Dr. H. Graham Hodgson.

Secretary-General—Dr. J. W. McLaren.

The program will be divided into four sections, each under the direction of a Vice-President, as follows:

Radiologic Diagnosis—Dr. S. Cochrane Shanks.

Radiotherapy—Prof. B. W. Windeyer.

Radiophysics—Prof. W. V. Mayneord.

Radiobiology—Dr. F. Gordon Spear.

The American Delegation is composed of representatives appointed by the four national radiological societies and by the Section on Radiology of the American Medical Association. The Members are:

American Roentgen Ray Society: Delegate, Dr. B. R. Kirklin, Mayo Clinic, Rochester, Minnesota; Alternate, Dr. E. L. Jenkinson, St. Luke's Hospital, Chicago 5, Illinois.

Radiological Society of North America: Dr. F. W. O'Brien, 465 Beacon Street, Boston 15, Massachusetts; Alternate, Dr. John D. Camp, Mayo Clinic, Rochester, Minnesota.

American Radium Society: Delegate, Dr. Douglas Quick, 350 Park Avenue, New York, N. Y.; Alternate, Dr. F. W. O'Brien, 465 Beacon Street, Boston 15, Mass.

Section on Radiology, American Medical Association: Delegate, Dr. U. V. Portmann, Cleveland Clinic, Cleveland 6, Ohio; Alternate, Dr. Edwin C. Ernst, 3720 Washington Boulevard, St. Louis, Missouri.

American College of Radiology: Delegate, Dr. Ross Golden, Presbyterian Hospital, New York 32, New York; Alternate, Dr. B. P. Widmann, 250 South 18th Street, Philadelphia 3, Pennsylvania.

At a meeting of the Delegation held at the Palmer House, Chicago on September 14, 1948, under the Chairmanship of Dr. Arthur C. Christie, President of the Fifth International Congress, Ross Golden was made Chairman of the American Delegation.

Travel Arrangements. The Officers of the Sixth International Congress in London selected Thomas Cook and Son as the official travel agency of this Congress. The American Delegation has also selected Thomas Cook and Son as the official travel agency, believing that the best coordination of arrangements on both sides of the Atlantic could be secured in this way. Thomas Cook and Son will make a reservation of space so that American members of the Congress who desire to do so may travel across the Atlantic as a group. Inquiries and reservations should be addressed to Mr. C. L. Hill, Thomas Cook and Son, 587 Fifth Avenue, New York 17, New York. *However, any individual is at liberty to make arrangements with a travel agency of his own choosing.* The officials of the Congress in London, as well as representatives of several travel agencies, have expressed the opinion that transatlantic travel will be unusually heavy in the summer of 1950, and have emphasized the importance of making *round trip reservations* as early as possible.

The Program. Details concerning the organization of the program have not yet been received from the London office of the Congress. They will be published later. Applications for a place on the program should be addressed to Dr. Ross Golden, Presbyterian Hospital, 622 West 168th Street, New York 32, New York.

REPORT OF A CASE OF AN ANOMALOUS LOBE OF THE LIVER

To the Editor:

The paper, "Report of a Case of an Anomalous Lobe of the Liver," by Norris M. Hardisty, Edward A. Kearney, and Frank P. Brooks, on page 486 of the October issue of the JOURNAL attracted my special interest, because the illustrations given resembled very much those of a number of cases which I had published many years ago. Unfortunately, I cannot agree with the interpretation the authors have given their findings.

In short, they have found a sharply defined, rounded soft tissue shadow, projecting from the right diaphragmatic contour into the pleural cavity. Diagnostic pneumo-

peritoneum showed that the soft tissue mass was part of the liver, and lying below a thinned part of the diaphragm. Subsequent operation confirmed the roentgen findings and revealed that apparently normal liver tissue was forming the mass. Roentgen examination after repair of the incision in the thinned area of the diaphragm showed that the projection was now smaller than preoperatively.

The fact that the diaphragm at the site of prominence was thinned should have indicated that a diaphragmatic hernia was present, containing liver. It is hardly conceivable how an anomalous lobe of the liver could cause atrophy of the diaphragm. On the other hand, after repair of the hernia the prominence was markedly reduced in size, and it is just as difficult to understand how suturing the diaphragm would reduce an anomalous liver lobe to half its original size.

Right diaphragmatic hernias having as only content a comparatively small portion of the—otherwise normal—liver are not extremely rare. I have reported 4 such cases in the *Fortschritte auf dem Gebiete der Röntgenstrahlen* in 1923, vol. 30, p. 305 and 473, and another case of "Hernia diaphragmatica dextra hepatis" in the *Fortschritte*, 1926, vol. 34, p. 481, and have discussed the differential diagnosis in *Wiener Archiv für innere Medizin*, 1923, vol. 6, p. 445, giving extensive literature references up to that date. Since that time I continue to see the condition at not too infrequent intervals. Originally I used diagnostic pneumoperitoneum to satisfy myself that the mass was continuous with the liver, and that the hernia usually was a true one; that is, that the serous membranes of pleura and peritoneum were preserved at least, even if the diaphragm muscle was defective to a greater or lesser extent (the last published case, however, was a false hernia, so that the pneumoperitoneum resulted in right pneumothorax). Eventually, however, I became convinced that the isolated paradoxical movement of the prominent part of the diaphragmatic contour (while the rest of it moves in a normal direction) is sufficient evidence for the presence of diaphragmatic hernia. But I have made it a point that nothing short of Müller's experiment (attempted forceful inspiration, while the glottis—or for that matter, mouth and nose—are closed) or one of its modifications is a reliable function test of the diaphragm. Merely forceful inspiration will disclose only the higher degrees of functional impairment of the diaphragm.

The anatomical literature on such hernias of the right diaphragm with liver as the only content is somewhat more abundant than the roentgenological literature. The liver is readily molded by the surrounding structures. The difference between abdominal and pleural pressures forces the adjacent part of the liver into the diaphragmatic defect and in some instances makes it mushroom on the upper surface of the diaphragm.

At postmortem examination a mushroom-like or peg-like process of the liver is found, fitting snugly into the pocket of the right pleural cavity. This prominent part of the liver shows the normal lobular architecture with central veins and bile ducts.

Such hernia diaphragmatica dextra hepatis is usually asymptomatic and only an incidental finding during a roentgen examination made for some other reason. Only in a minority of cases there are symptoms which could be referred to the hernia. There are, however, never complications requiring surgery, such as is the case if hollow viscus or omentum is the content of a diaphragmatic hernia.

Hernia diaphragmatica dextra hepatis is either acquired or—more often—congenital. Since in the histories of most adults some trauma can be found which may possibly be etiological, the typical or atypical location of the hernia will give a hint as to whether it is due to developmental abnormality or to injury. At any rate, such hernias have been described in infants, which is always a strong indication that the abnormality is developmental.

Incidentally, such liver hernias are not confined to the right leaf of the diaphragm. Keith (*Brit. M. J.*, 1910, p. 1297) has found

liver herniated into the pericardial cavity, and other authors have described similar abnormalities in dogs.

LEO REICH, M.D.

2242 Independence St.
Phoenix, Arizona

To the Editor:

In reply to Doctor Reich's letter commenting on the "Case Report of Anomalous Lobe of the Liver," I wish to state that it is, perhaps, noteworthy that so far, he is the only one who has seen fit to indulge in written comment on the report. I am unable to read German and it is entirely possible that certain foreign publications have not been included in our list of references.

It would appear that Doctor Reich and we are looking at the problem from different angles. I feel that Doctor Reich is entitled to his opinion if he chooses to consider the condition as a form of hernia involving the diaphragm. The other authors and I considered the primary condition to be an anomalous lobe of the liver and the overlying thinning of the diaphragm to be of secondary moment. The fact that the diaphragm was found to be intact after pneumoperitoneum and surgery definitely denies the existence of a hernia and definitely establishes the presence of a localized eventration. The fact that herniation of the liver through the diaphragm does occur is not questioned and the fact remains in this case that only that portion of the diaphragm overlying this anomalous lobe seemed to be thin and eventrated. We were definitely of the opinion that this anomalous and pedunculated liver lobe was the probable cause of the local thinning and stretching of the diaphragm. At operation the anomalous lobe was not protruding through the diaphragm in the ordinary sense but was pressing it upward. The thinned diaphragm was shortened by plicating it and suturing it. We expected that the tightened diaphragm would flatten this lobe, at least for a time after operation.

In this instance, I fail to appreciate the premise that the diaphragm was locally weak and that the liver forced a portion of its substance as a pedunculated mass through the diaphragmatic weakness. There was no break in the diaphragm and, therefore, no hernia.

N. M. HARDISTY
Captain (MC) USN

U. S. Naval Hospital
St. Albans 12, N. Y.

LOS ANGELES RADIOLOGICAL SOCIETY

At a recent meeting of the Los Angeles Radiological Society the following officers were elected to serve for the ensuing year: *President*, Dr. John McAtee; *Vice-President*, Dr. Leo Levi; *Secretary*, Dr. Wybren Hiemstra; Treasurer, Dr. Wilbur Bailey.

ROCHESTER ROENTGEN RAY SOCIETY

At the annual meeting of the Rochester (N. Y.) Roentgen Ray Society in December, 1948, the following officers were elected for the coming year: *President*, Dr. George H. Ramsey; *Vice-President*, Dr. E. Forrest Merrill; *Secretary-Treasurer*, Dr. Ralph E. Alexander.

CORRECTION

The need for a correction in the paper by A. U. Desjardins, F. A. Figi, and L. M. Vaughan, "Roentgen Treatment for Extensive Epithelioma of the Larynx," AM. J. ROENTGENOL. & RAD. THERAPY, July, 1948, *60*, 29–36, has been discovered by the authors. The corrections have to do with the first two sentences of the last paragraph of the paper, and should read as follows:

From Table 1 it may be seen that, out of 139 cases in the entire series, 71 patients were treated between 1936 and 1942, inclusive; of these we have not been able to obtain information concerning 3 cases (although the probable outcome in these 3 cases is recorded in Table 1). This leaves 68 patients in this series who were treated during this period and of whom 14 are living five years or more since their treatment at the Clinic.

VOL. 61, NO. 2

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

Department Editor: GEORGE M. WYATT, M.D., 1835 Eye St., N.W., Washington 6, D. C.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

WEENS, H. S.: Calcified intracranial tuberculomas 262

BAILY, O. T., INGRAHAM, F. D., NEUHAUSER, E. B. D., and COBB, C. A., Jr.: Fibrin film in neurosurgery, further studies 263

OSCHERWITZ, D., and DAVIDOFF, L. M.: Midline calcified intracranial aneurysm between occipital lobes 263

COLEMAN, C. C., and TROLAND, C. E.: Congenital atresia of the foramina of Luschka and Magendie 263

ECKER, A.: Upward transtentorial herniation of the brain stem and cerebellum due to tumor of the posterior fossa 264

TORKILDSEN, A.: Spontaneous rupture of cerebral ventricles 264

LIST, C. F., and HODGES, F. J.: Differential diagnosis of intracranial neoplasms by cerebral angiography 265

LINDGREN, E.: Technique of direct (percutaneous) cerebral angiography 266

Neck and Chest

NEUHAUSER, E. B. D., and BERENBERG, W.: Cardio-esophageal relaxation as a cause of vomiting in infants 266

KRISTOFF, F. V., and DRATZ, H. M.: Minor fractures of cervical laminae simulating ruptured cervical disk 267

BUCY, P. C., and RITCHEY, H.: Klippel-Feil's syndrome associated with compression of the spinal cord by an extradural hemangiolipoma 267

SELDIN, D. W., KAPLAN, H. S., and BUNTING, H.: Rheumatic pneumonia 268

GARLAND, L. H.: Pulmonary sarcoidosis 268

GREENING, R. R., and MENVILLE, L. J.: Roentgen findings in torulosis 269

JAMISON, H. W., and CARTER, R. A.: Roentgen findings in early coccidioidomycosis 270

HOLLINGSWORTH, R. K.: Bronchiogenic carcinoma 271

HEUBLEIN, G. W., and GILFILLAN, C. D. N.: Practical technic for visualization of the bronchial tree 272

LAM, C. R.: Pericardial celomic cysts 272

SOSMAN, M. C.: Venous catheterization of the heart. I 273

DEXTER, L.: Venous catheterization of the heart. II 273

HOLT, J. F.: Epipericardial fat shadows in differential diagnosis 274

BATT, R. C.: Roentgenkymographic study of the heart in myasthenia gravis 274

CLARK, S. B., and KOENIG, E. C.: Aortic aneurysm secondary to coarctation 275

O'LOUGHLIN, B. J.: Study of 24,615 separation chest roentgenograms 275

EPSTEIN, B. S.: Rheumatic mitral valve disease without cardiac enlargement 275

UNGERLEIDER, H. E.: Cardiac enlargement 275

Abdomen

GERSHON-COHEN, J.: Duodenal mechanism regulating the motor and secretory activity of the stomach 277

OULD, C. L., and DAILEY, M. E.: Simultaneous radiographic and gastroscopic examination of the stomach 277

ZANCA, P.: Gastrocolic fistula complicating carcinoma of the colon 278

EUPHRAT, E. J.: Roentgen features of mucocele of the appendix 278

BREWER, A. A.: Cholecystography 278

RIGLER, L. G., and MIXER, H. W.: Cholangiography and biliary regurgitation 279

Gynecology and Obstetrics

SCARPELLINO, L. A.: Cephalopelvimetry 279

Genitourinary System

MYERS, L. A.: Range of usefulness of intravenous pyelography 280

Nervous System

SCOVILLE, W. B., MORETZ, W. H., and HANKINS, W. D.: Discrepancies in myelography 280

DENNY-BROWN, D.: Primary sensory neuropathy with muscular changes associated with carcinoma 281

Skeletal System

GILMORE, J. H., and MAHAN, T. K.: Case of acromegaly presenting specific roentgenographic changes 281

GALLUCCIO, A. C.: Observations on gunshot fractures of mandible 281
COOPER, G., JR., ADAIR, N., and PATTERSON, W. M.: Familial osseous atrophy 281
RUSSO, P. E.: Malignant melanoma in infancy 282

ROENTGEN AND RADIUM THERAPY

McINDOE, A. H., FORBES, R., and WINDEYER, B. W.: Symposium: radiation necrosis 282
CROSS, J. E., GURALNICK, E., and DALAND, E. M.: Carcinoma of the lip 283
RICHARDSON, W., and ROBBINS, L. L.: Treatment of pylocythemia vera by spray irradiation 284
POHLE, E. A., and TOMLINSON, C.: Roentgen therapy in traumatic myositis ossificans 284
DEL REGATO, J. A.: Role of transvaginal roentgen therapy in treatment of carcinoma of cervix 285
SAUER, H. R., WATSON, E. M., and BURKE, E. M.: Tumors of the testicle 285
BERMAN, L., and AXELROD, A.: Effect of urethane on malignant diseases 286
HERRMANN, J. B., ADAIR, F. E., and WOODARD, HELEN Q.: Effect of estrogenic hormone on advanced carcinoma of female breast .. 286

MISCELLANEOUS

MARTIN, J. H.: Radiation doses received by skin of a patient during routine diagnostic x-ray examinations 286
MITCHELL, J. S.: Experiments on mechanism of biological action of fast neutrons using summation method for lethal effects in mice 287
LEWIS, MARGARET, R.: In vivo staining and retardation of tumors in mice by acridine compounds 287
LASNITZKI, ILSE: Quantitative analysis of direct and indirect action of x radiation on malignant cells 287
WOLFF, BRIGITTE, and ELLIS, F.: Quantitative histological analysis of radiation effects in human carcinomata 288
HOWARTH, F.: Isotopes and radiation hazards 288
MOORE, F. D.: Use of isotopes in surgical research 288
ELKIN, D. C., COOPER, F. W., RORHER, R. H., MILLER, W. B., SHEA, P., and DENNIS, E. W.: Study of peripheral vascular disease with radioactive isotopes 289
SIEVERT, R. M.: Tolerance dose and prevention of injuries caused by ionizing radiations 289

ROENTGEN DIAGNOSIS

HEAD

WEENS, H. S. Calcified intracranial tuberculomas. *J. Pediat.*, Sept., 1948, *33*, 328–335.

A recent review by Wilson and Bruce indicates that intracranial tuberculomas constitute 3.5 per cent of verified brain tumors. About one-half of the cases occurred in patients under ten years of age. Calcifications occur infrequently in these lesions. This is contrary to most tuberculous lesions. Since surgical removal of these tumors may be of value it is important to be able to identify them.

The author reports 3 cases in children with illustrative films. The diagnosis was proved in only 1 of the 3 cases. Calcified tuberculomas of the brain vary in size from a few millimeters to 2–3 cm. The lesions are usually solitary, but may be multiple. One of the author's cases had eleven tuberculomas which is more than has ever been reported.

A characteristic roentgen appearance of the calcium deposits in tuberculomas, based on their gross shell-like structure, is described. The calcifications are homogeneous in the center with lace-like angular margins. In some cases small spicules of calcium seem to be separated from the calcified center. Among the other lesions to be considered in a differential diagnosis are craniopharyngiomas, and angiomas. In craniopharyngiomas the calcifications are in the region of the pituitary fossa which is usually enlarged. Calcifications in angiomas usually have a typical double contour with a tortuous racemose pattern. Characteristically they are found in the occipital area. The calcification in subdural hematomas is usually strandlike and close to the inner table of the skull. Ependymomas are difficult to distinguish from tuberculomas by roentgen examination.

The calcifications in tuberous sclerosis are also to be considered in the differential diagnosis. These are usually smooth and discrete and in close relationship to the ventricular system. The cutaneous manifestations of this syndrome help to differentiate it.

The calcifications found in toxoplasmosis may be differentiated by their small size and the associated chorioretinitis and hydrocephalus.

Among rarer causes of intracerebral calcifications are bilateral symmetrical calcifications of the basal ganglia. Tuberculomas may be entirely asymptomatic.—*Rolfe M. Harvey, M.D.*

Baily, Orville T., Ingraham, Franc D., Neuhauser, Edward B. D., and Cobb, Cully A., Jr. Fibrin film in neurosurgery, further studies; the insertion of fibrin film between the sutured dura and the intact leptomeninges; the effect of roentgen therapy on tissue reactions to fibrin film. *J. Neurosurg.*, Sept., 1947, *4*, 465–471.

In operations where the brain and dura are traumatized or sections of dura are removed, it is desirable to close the dural defect with fibrin film. To test whether this material should be used following intracranial operations in which the dura is completely closed after little manipulation of the brain and leptomeninges, the authors have performed temporoparietal craniotomies in monkeys with and without insertion of fibrin film under the sutured dura. These experiments show that in the monkey uncomplicated craniotomies produce adhesions under the sutures used to close the dura. Fibrin film prevents this complication.

It is often desirable to use fibrin film in patients who may later require roentgen therapy. The possibility that roentgen rays may change the fibrin film itself or the reaction of tissues to it made it desirable to study the effect of roentgen rays on the tissue reaction to this material. A strip of sterilized fibrin film was moistened with saline and then exposed to the contact roentgen therapy apparatus. The total roentgen dosage was 8,000 r (measured in air). This fibrin film was then submitted to the tests which have been used to standardize this material. The roentgen rays could not be said to have changed the physical characteristics of the film. Experimental studies on monkeys and also inspection of operative wounds and autopsy material of human subjects showed that roentgen therapy in the doses used for treatment has no detectable effect on fibrin film or the reaction of the meninges to this material.—*K. K. Latteier, M.D.*

Oscherwitz, Daniel, and Davidoff, Leo M. Midline calcified intracranial aneurysm between occipital lobes; report of a case. *J. Neurosurg.*, Nov., 1947, *4*, 539–541.

Intracranial aneurysms nearly always arise from arteries at the base of the brain in the vicinity of the circle of Willis. In rare instances they may be located out along the larger branches of the circle and lie imbedded in the brain substance. The authors report the occurrence of a calcified aneurysm situated in the midline between the occipital lobes. The patient, a female, aged twenty-seven, complained of headaches of nine months' duration and intermittent blurring of vision. Neurological examination was entirely negative. Roentgenograms of the skull revealed a large, round and somewhat irregular cyst-like mass with calcified borders measuring 3.5 cm. in diameter lying in the midline just posterior and superior to the pineal gland. Ventriculograms revealed a normal ventricular system except for a slight indentation on the inner aspects of both posterior horns. Operation demonstrated a calcified aneurysm lying between the occipital lobes and probably representing an arteriovenous aneurysm of the vein of Galen and the branches of the circle of Willis.

The literature revealed only 4 cases of vascular anomalies similar to this case; 2 of these were found in infants. Calcification was also present in only one of these cases.—*K. K. Latteier, M.D.*

Coleman, Claude C., and Troland, Charles E. Congenital atresia of the foramina of Luschka and Magendie; with report of two cases of surgical cure. *J. Neurosurg.*, Jan., 1948, *5*, 84–88.

An excellent presentation of the entire subject of atresia of the foramina of Luschka and Magendie was given by Taggart and Walker in 1942. They reviewed the literature and detailed the development of these foramina and the vermis of the cerebellum. On the basis of these studies, they presented a roentgenographic picture that is pathognomonic of the condition. Coleman and Troland present 2 additional cases which do not show these typical findings of the impression of the confluent and lateral sinuses on the parietal bone and a high inion. In the first case, a fourteen month old female infant, the roentgenograms showed marked increase in the size of the calvarium, and

convolutional atrophy that was most marked in the parietal and occipital regions. The inion was in approximately normal position. The second case, that of a seventeen year old white male, showed marked convolutional atrophy with a large cranial vault but no widening of the sutures. Ventriculography revealed dilatation of both lateral ventricles and the 3rd ventricle. There was no air in the 4th ventricle and the impression was that of a posterior fossa lesion, probably congenital.

It is obvious that equilibrium must be established between the production of fluid in the ventricles and its escape into the subarachnoid system for this condition to be compatible with life. It is probable that in the cases reported here, this equilibrium was established early enough to permit posterior migration of the venous sinuses. Surgical treatment should be performed as soon as possible in order to prevent cortical atrophy.—*K. K. Latteier, M.D.*

ECKER, ARTHUR. Upward transtentorial herniation of the brain stem and cerebellum due to tumor of the posterior fossa; with special note on tumors of the acoustic nerve. *J. Neurosurg.*, Jan., 1948, *5*, 51–61.

Localized increases of intracranial pressure commonly displace parts of the brain in relation to both the skull and its dural partitions. Data from the literature and 2 illustrative cases indicate an upward herniation of the brain stem and cerebellum through the incisura tentorii in most cases of posterior fossa tumor. Such herniation might be called the inverted tentorial pressure cone or upward transtentorial herniation. Identical ventriculograms may be obtained in cases of tumor of the cerebellum, pons or floor of the third ventricle. As an illustration the author presents the case history of a two and a half year old child where ventriculography revealed huge bilateral dilatation of the lateral ventricles and of the anterior aspect of the 3rd ventricle. There seemed to be a large space-occupying mass in the posteroinferior portion of the 3rd ventricle, with complete blocking of the aqueduct at its origin. Third ventriculostomy was performed, but no tumor was seen in the floor of the 3rd ventricle. Later a solid cerebellar tumor was found in the midline between the cerebellar tonsils. Autopsy revealed that the rostral portion of the cerebellum was pushed upwards through the tentorial notch. Furthermore, the cerebral peduncles had been displaced upward, thus accounting for the defect on the posterior portion of the 3rd ventricle.

In acoustic nerve tumors, bulging of and herniation through the tentorium may compress the inferior surface of the temporal lobe so as to obliterate the lumen of the temporal ventricular horn. It may also cause lateral compression of the lower portion of the 3rd ventricle, simulating in the lateral ventriculogram a tumor of the 3rd ventricle. Finally, it may elevate the first portion of the middle cerebral artery. The roentgenograms of the skull in the case of acoustic nerve tumor described by the author suggested that the left internal auditory canal was larger than the right and that the pineal body was calcified and displaced very slightly upward. Despite the use of special maneuvers, there resulted no filling with air of the inferior portion of the 3rd ventricle, aqueduct or 4th ventricle. Later an autopsy revealed a typical left acoustic neurinoma. It had displaced the brain stem and cerebellum to the right and upward.

At the time of autopsy there was no immediate explanation for the non-filling of the inferior and posterior aspects of the 3rd ventricle. Further study of the lateral view of the ventriculogram revealed an apparent round defect, convex upward, simulating a tumor in the lower three-fourths of the 3rd ventricle and identical with that of another case of tumor of the pons. Secondly, the left temporal horn was not filled at all. The tumor in this case caused complete obliteration of both the left temporal horn and the lower three-fourths of the 3rd ventricle.—*K. K. Latteier, M.D.*

TORKILDSEN, ARNE. Spontaneous rupture of the cerebral ventricles. *J. Neurosurg.*, July, 1948, *5*, 327–339.

Relative intraventricular hypertension may result when resorption of the cerebrospinal fluid does not equal the rate of production. With occlusion of the foramina of Monro, a relative hypertension exists within the lateral ventricles, and with occlusion of the Sylvian aqueduct, relative hypertension exists within the lateral ventricles and the 3rd ventricle as compared with the pressure in the subarachnoid space. Under such abnormal tension a rupture of the ventricular wall may take place. The result of such a rupture depends entirely upon the details concerning its location and its relationship to the membranes covering the central nervous system. Two favored locations

for the breakdown of the ventricular wall seem to be the mesial wall of the temporal horn where it joins the posterior horn and the body of the lateral ventricle, and the anterior or posterior wall of the 3rd ventricle.

The author describes 5 cases of spontaneous rupture of the cerebral ventricular system. In 4 cases the rupture resulted in the formation of a cyst occupying the interpeduncular space, extending below the tentorium and covering the quadrigeminal plate. One case differs from the others inasmuch as the rupture did not create a cyst below the tentorium. After the spontaneous rupture the cerebrospinal fluid filled the supratentorial subdural space on the left side, resulting in an accumulation of the cerebrospinal fluid causing cerebral compression.

Spontaneous rupture of the cerebral ventricles is a pathological anatomical condition which is easily diagnosed by ventriculography. The presence of cyst formation frequently indicates a pathological condition that can be treated advantageously by ventriculocisternostomy.—*K. K. Latteier, M.D.*

List, Carl F., and Hodges, Fred J. Differential diagnosis of intracranial neoplasms by cerebral angiography. *Radiology*, May, 1947, *48*, 493–508.

In a series of 125 patients with intracranial tumor subjected to angiography at the University of Michigan Hospital a special vascular pattern was observed in the angioma, meningioma and glioblastoma groups as well as in certain types of astrocytoma.

A. *Angioma Group* (8 cases).

1. Arteriovenous malformations (6 cases).

By angiography there can be demonstrated one or several enlarged and unusually tortuous arteries leading to a tangle of smaller vessels forming a more or less well defined mass from which one or more greatly dilated redundant veins emerge. The entire malformation fills during the arterial phase of angiography. Arteriovenous malformations may be bilateral and most frequently involve anterior and middle cerebral arteries. The uninvolved cerebral vessels are not displaced. Associated cardiac hypertrophy and enlargement is occasionally demonstrated.

2. Cavernous angiomas (2 cases).

These rather rare lesions usually are of small size. Angiography has been disappointing in 2 cases.

3. Angioblastomas.

These occur almost exclusively in the cerebellum and have not been studied by angiography.

B. *Meningioma Group* (20 cases).

Meningiomas possess a rich blood supply derived from the external carotid system and from the internal carotid (and vertebral) system. A positive image of the dural blood supply can be obtained by arteriography of the external carotid artery. Following injection of the internal carotid artery, the cortical arteries in contact with the tumor appear to be distended and separated from one another, whereas the arteries of the adjacent compressed brain are crowded together and form a concentrically arranged corona around the lesion. In addition, there are seen one or multiple newly formed tumor vessels. The latter are usually rather small arteries splitting into fine branches within the meningioma and their appearance by angiography has been compared to a paint brush or flower spray. On the venogram, tumor veins appear as large short veins with many tributaries, and they tend to outline the circumference of the growth. A typical feature is the diffuse uniform or slightly mottled opacity of the tumor attributed to visualization of a fine network of vessels of capillary or near capillary size.

Diffuse radiopacity may be visible in the arterial phase (1–1.5 sec.) in meningiomas near the carotid siphon whereas it appears in the venous phase (3–5 sec.) in tumors located elsewhere.

C. *Glioblastoma* (55 cases).

Due to the infiltrating manner of tumor growth displacement of cerebral vessels tends to be more diffuse and less profound than with meningiomas of comparable size. Two types of special vascular pattern are seen in glioblastoma. The first is an irregular network of fine criss-crossing vessels and a few larger sinusoid vessels which produce lacunar dilatations with spiral or corkscrew patterns. The second is characterized by a very coarse and bizarre vascular pattern resembling an arteriovenous malformation. The large malformed vessels, probably sinsoids and veins, may form spirals or arrange themselves in parallel layers in the tumor. Well defined aberrant arteries and ef-

ferent veins, characteristic of arteriovenous malformations are not seen in glioblastomas. Some glioblastomas having necrotic or cystic centers are similar to meningiomas in appearance.

D. *Astrocytomas* (12 cases).

The blood supply of an astrocytoma is relatively scanty and is not demonstrated too well by either angiographic or histopathologic methods. Angiograms show stretching and spreading of the larger and medium sized cerebral arteries. Finer arterial branches which are always visible in the normal may be entirely absent. Frequent presence of cysts is one factor to account for sparseness of vessels. The angiogram of diffuse astrocytoma resembles that seen in brain edema.

E. *Other Types of Intracranial Neoplasms.*

The authors' experience with angiography has not been sufficiently large to describe a specific vascular pattern in certain of the rarer intracranial neoplasms.—*John R. Hannan, M.D.*

LINDGREN, E. The technique of direct (percutaneous) cerebral angiography. *Brit. J. Radiol.*, August, 1947, *20*, 326–331.

Three important points in cerebral angiography are the technique of puncture, the opaque material, and the roentgenographic technique. All three are discussed in more or less detail. The puncture is made usually under local anesthesia and an attempt is made to palpate the vessel with the tip of the needle while the needle is in the tissues. The internal, external, or common carotid may be used as needed.

Thorotrast is used in patients who have no voluntary control, but in all others umbradil is used. Thirty-five per cent or 50 per cent solutions are used, depending on the amount of dilution by the blood to be expected, and upon the response of the patient to the weaker solution.

The apparatus used consists of a holder which keeps three films against the side of the patient's head and three underneath while he is supine with the neck in hyperextension. Lysholm grids are used. This apparatus permits anteroposterior and lateral views without moving the patient. Films are made after each of several injections of 8 or 9 cc. of the opaque material in lateral and anteroposterior views.

By this method 153 patients were examined in an eighth month period with 4 technical failures and no serious ill effects. This procedure has been carried out on out-patients.—*E. F. Lang, M.D.*

NECK AND CHEST

NEUHAUSER, EDWARD B. D., and BERENBERG, WILLIAM. Cardio-esophageal relaxation as a cause of vomiting in infants. *Radiology*, May, 1947, *48*, 480–483.

Persistent or recurrent vomiting in the newborn or young infant occurs as a frequent problem in pediatric care. There is a considerable number of patients in whom, because of the repeated and significant nature of the vomiting, roentgenologic examination is warranted. Among this group the authors have observed, in the past three years, 12 patients who exhibited persistent vomiting, evidently due to relaxation or dysfunction of the hiatus portion of the esophagus with failure of the normal "sphincter" action of the cardia. One could postulate that this type of persistent relaxation might be the result of failure of the pinchcock mechanism to function adequately, due to failure of proper development or to imbalance of neuromuscular control.

The patient almost invariably starts vomiting within a week after birth, usually during the first few days of life. The vomiting becomes progressively worse and soon occurs with each feeding. The vomiting may take place during a feeding, especially when air is expelled, but is most apt to occur when the child is put back in his crib in the supine or decubitus position. The diagnosis of cardio-esophageal relaxation depends almost entirely on an adequate fluoroscopic examination of the swallowing function, esophagus and stomach. The barium-filled esophagus usually appears larger than would be considered normal. Some relative narrowing of the hiatus esophagus is observed, but there is persistent failure of the "pinchcock" or "sphincter" action to come into play, so that the esophagus appears as a rather flaccid tube leading to the cardiac end of the stomach. During the inspiratory phase of respiration the esophagus dilates and frequently will fill with barium from the stomach. With expiration the filled esophagus is compressed; some of the barium passes again into the stomach and some is regurgitated into the mouth. When the patient is in the supine position, even slight pressure upon the abdomen will produce retro-

grade filling of the esophagus with air or barium from the stomach. If the patient is observed in the erect position, no regurgitation takes place, although it is usually evident that the hiatus esophagus is open, as frequently one can observe air passing into the esophagus from the stomach.

Treatment of this condition has been empiric. The patients are fed in the sitting or erect position and maintained in this position for thirty minutes after the feeding has been accomplished. In the presence of well defined persistent relaxation, the authors have, in addition, kept the infant propped up and maintained in a semi-sitting position in its crib throughout the day and night. On such a regimen all of the infants stopped vomiting almost immediately and showed good weight gain and normal development.—*Samuel G. Henderson, M.D.*

Kristoff, Frederic V., and Dratz, Henry M. Minor fractures of the cervical laminae simulating ruptured cervical disk; report of two cases. *J. Neurosurg.*, Jan., 1948, *5*, 95–98.

From a differential diagnostic standpoint the lesions described herein are of considerable interest as they at times may simulate the syndrome of a ruptured cervical disc. These factures are minor lesions unless accompanied by cord damage, or occur near the intervertebral foramen. When the intervertebral foramen is involved the fracture is apt to affect the corresponding nerve root on its course through the foramen, thus reproducing the clinical picture of a laterally ruptured disc. Two cases are presented; both were diagnosed clinically as ruptured cervical disc and both patients were successfully operated upon.

The complaints caused by these fractures are identical to those of a ruptured disc, e.g., pain in the neck on motion of the head and radicular pain referable to one root. The objective signs are also identical, e.g., the mechanical signs, present in order to immobilize the fracture, and the neuropathological signs caused by damage of one nerve root. An immediate onset of the above symptoms and signs is the rule when the problem is that of a laminar fracture, whereas the same may have a latent period of variable duration when associated with a ruptured disc.

Roentgenograms of the neck should be taken in stereoscopic views, the anteroposterior, the lateral and oblique exposures, in order to obtain better visualization of detail. However, plain oblique views, taken of both sides for comparison, may be of great aid in directing the surgical approach by showing distinctly either a small bone fragment protruding into the intervertebral foramen in question, or a unilateral disfiguration of same. Myelography is unnecessary if the plain roentgenograms are carefully made. The myelogram may, or may not, show a filling defect in the contrast shadow, giving no lead as to etiology, however.—*K. K. Latteier, M.D.*

Bucy, Paul C., and Ritchey, Hardin. Klippel-Feil's syndrome associated with compression of the spinal cord by an extradural hemangiolipoma. *J. Neurosurg.*, Sept., 1947, *4*, 476–481.

Klippel-Feil's syndrome is a congenital malformation of the neck characterized by a fusion of many of the cervical vertebrae and a reduction in the number of bony components of the cervical spine. There may be an absence of the spinous processes and laminae and also associated neurological abnormalities. When these are present they are usually due to compression of the spinal cord or its roots by bony malformations or a result of malformations of the spinal cord itself. The case reported by the authors is of interest as there was typical clinical evidence of an intraspinal tumor and this was confirmed at operation.

A man, aged thirty-three, had been aware of a deformity of his neck all of his life, but this had caused him little disability. In the course of ten weeks he developed signs of compression of the upper thoracic spinal cord which rapidly progressed to a total paraplegia.

The roentgen examination of the cervical and upper thoracic spine revealed a solid fusion of the 2nd, 3rd, 4th, and 5th cervical vertebrae. The 6th and 7th cervical vertebrae and the first five thoracic vertebrae were fused into a similar long solid mass. The pedicles of the first four thoracic vertebrae were either congenitally absent or had been eroded.

Operation disclosed a friable vascular tumor which compressed the dura mater and the spinal cord. Microscopic examination of the tumor showed a tissue which was basically lipomatous, and scattered through the lipomatous tissue were many vascular channels. The tumor was regarded as a hemangiolipoma.

The authors feel that there can be little doubt but that the extradural hemangiolipoma

which resulted in the compression of the spinal cord in this case and which was responsible for the neurological symptoms was the result of a congenital malformation. Why it did not give rise to evidence of its presence for thirty-three years is as obscure as is its etiology.—*K. K. Latteier, M.D.*

SELDIN, DONALD W., KAPLAN, HENRY S., and BUNTING, HENRY. Rheumatic pneumonia. *Ann. Int. Med.*, April, 1947, *26*, 496–520.

Although the existence of a true pulmonary component of the rheumatic process has been denied, the literature contains enough material to establish the presence of characteristic changes labeled by many as a rheumatic pneumonia. This pathologic process is peculiar to rheumatic activity and is not considered to be the result of such complications as infarction, atelectasis, or intercurrent infection. The precise relationship to rheumatic fever, however, is still obscure. From the various sources in the literature, four hypotheses are offered to explain these pulmonary changes:

1. The lesions are specific manifestations of rheumatic activity in the lungs.
2. The changes are secondary to congestive heart failure.
3. The changes are the result of intercurrent infection.
4. A combination of rheumatic activity and cardiac failure might account for these changes.

In the present series, the authors analyze 6 cases in an effort to bring forth criteria by means of which a clinical and roentgen diagnosis of rheumatic pneumonia might be ventured. In 4 of the cases, serial roentgenograms are reproduced to show the course of the pulmonary process. All of the prominent symptoms and signs are reviewed in detail. Necropsy reports are present on all of the cases. It is emphasized that in all cases the clinical, laboratory, and anatomical evidence of rheumatic carditis was present.

Several photomicrographs of the pathological sections of the involved portion of the lungs are reproduced to illustrate the so-called typical findings. The main points to be noted are: (1) thickening of the alveolar walls and interstitial tissues by cellular infiltrations, proliferation of endothelial cells, and capillary congestion; (2) alveolar exudate which is hemorrhagic in nature; (3) bronchioles lined by a hyaline pseudo-membrane. Typical Aschoff's bodies have been reported by one group.

Clinically, there are two fairly well recognized syndromes. In the first type, the pulmonary symptoms develop insidiously. Toxicity is not great and the temperature is only moderately elevated. Although the respiratory symptoms are minimal, physical signs are striking by comparison. In the second group, however, the pulmonary involvement is rapid and widespread. Dyspnea and cyanosis quickly appear and the case may terminate fatally.

The roentgen changes in the cases presented fell into three fairly well defined categories. These changes were: vascular engorgement, pulmonary congestion and pulmonary edema. The latter finding was the most common. Despite the prominence of the roentgen changes, however, the authors stressed that by this means alone one cannot make the diagnosis of rheumatic pneumonia. Suitable clinical studies are necessary. However, with this combined information, one can usually eliminate the bacterial and primary atypical pneumonic consolidations. The most difficult problem, of course, consists in distinguishing the changes from the various phases of cardiac failure.

In the closing discussion, the authors reiterate that the clinical and roentgenologic criteria for the diagnosis of rheumatic pneumonia are still inconclusive and postmortem verification is necessary. This, of course, makes difficult the evaluation and prognosis in the suspected milder cases. As all the cases in this series terminated fatally, it is fair to assume that the manifestations presented would carry a very grave prognostic significance.—*Robert N. Byrne, M.D.*

GARLAND, L. HENRY. Pulmonary sarcoidosis: the early roentgen findings. *Radiology*, April, 1947, *48*, 333–354.

Sarcoidosis is a generalized disease of unknown origin, in which characteristic histopathologic changes are found in different organs and tissues. It is usually of insidious onset and tends to run a chronic, relapsing course. It is discovered most commonly between the ages of twenty and thirty years.

It is often observed in a phase when involvement of only one system is apparent; for example, lesions of the skin, the eyes, or the lungs. Peripheral lymphadenopathy is present at some stage of the disease in about 90 per cent of the

cases, the nodes being painless, discrete, and movable. Pulmonary involvement (parenchymal or nodal) occurs in a similar percentage of cases. Cutaneous and ocular lesions are seen in about 40 per cent of cases. The usual skin lesions are described as sharply defined, browning nodules (cutaneous or subcutaneous) distributed over the face or extremities. Hepatomegaly and splenomegaly are fairly frequent. Cardiac and pericardial involvement has been noted. As in Hodgkin's disease, *any* tissue or structure can be invaded.

Granulomatous invasion of the bone marrow is fairly common. In a small percentage of cases, multiple radiolucent areas or diffuse lace-like rarefactions appear most commonly in the phalanges of the hands and feet, but may occur in any bones, notably the long bones of the extremities. Hyperglobulinemia, with reversal of the albumin-globulin ratio, is a common finding; eosinophilia is not infrequent. The serum calcium and phosphatase values may be slightly increased.

The tuberculin reaction is usually negative. The diagnosis is made in vivo by the demonstration of a non-caseating or "hard" tubercle in a biopsy specimen, usually from a node or skin nodule. The conditions with which sarcoidosis is most often confused are tuberculosis and Hodgkin's disease.

Gross and microscopic lesions similar to those in sarcoid have been found in some zinc-beryllium-silicate workers (fluorescent lamp manufacturers, etc.).

Chest roentgenographic findings in 36 cases of sarcoidosis are presented, 33 of which were verified by histopathologic examination, and 3 so well established clinically that the diagnosis appears valid.

In the thoracic roentgen film, certain patterns are quite suggestive of pulmonary sarcoidosis. In order of frequency, these are:

(a) Bilateral hilar and right paratracheal adenopathy, with or without associated pulmonary infiltration or nodular densities.

(b) Widely disseminated pulmonary miliary or nodular densities without calcification, in a person clinically well.

(c) Massive enlarged hilar nodes (potato nodes) in an apparently well person.

There is absolutely nothing characteristic in the findings in the individual case. The apparent excellent health of the person in contrast with the extensive roentgen shadows often warrants a surmise of sarcoidosis. The miliary and nodular lesions are due to aggregations of sarcoids in the lung parenchyma. The linear lesions may be due to sarcoid lymphangitis, to lymphedema, to congestion or occasionally to fibrotic changes.

Pulmonary lesions alone, without visible hilar or mediastinal adenopathy, were present at the initial examination in 10 cases.

Pulmonary lesions and lymphadenopathy were present at the initial examination in 13 cases. Six showed diffuse or localized nodular lesions with adenopathy. Seven showed diffuse or localized linear densities with adenopathy.

Lymphadenopathy, hilar, mediastinal, or both, was present as the sole thoracic roentgen finding at the initial examination in 11 cases. Six showed bilateral hilar plus *right* paratracheal adenopathy; 3 showed hilar adenopathy alone; and 1 each paratracheal adenopathy alone, and hilar plus left paratracheal adenopathy.

Pleural effusion was present in only one case.

The intrathoracic lymph node enlargement tends to conform to a curious pattern in which simultaneous enlargement of *both sets of hilar nodes* and only the *right upper mediastinal or paratracheal nodes* occurs. This was found in 7 of the cases with combined parenchymal and nodal lesions, and in 6 of the cases with nodal lesions alone. This has been suggested as "sarcoid-type" adenopathy.

A palpable lymph node or skin nodule is the most desirable tissue for microscopic examination. However, when *none* such is evident, exploration of the mesial end of the right supraclavicular fossa through a short incision will frequently yield *an upper anterior mediastinal node* for study and positive diagnosis.

The miliary type of pulmonary sarcoidosis occurred as an early finding in a minority of the cases.—*Stephen N. Tager, M.D.*

Greening, Roy R., and Menville, Leon J. Roentgen findings in torulosis; report of four cases. *Radiology*, April, 1947, *48*, 381–388.

Greening and Menville discuss torulosis and report 4 cases among 537,135 admissions to Charity Hospital, New Orleans, in a ten year period. There is an excellent summary of the literature and a discussion of the bacteriology and pathology of the disease. Involvement of the central nervous system is predominant and involvement of the lungs relatively rare. Incidence is highest between the ages of thirty and sixty. Meningeal irritation, increased intra-

cranial pressure, and a low grade fever are the chief clinical manifestations. Various neurological symptoms may be present. The presence of enlarged nodes may lead to confusion with Hodgkin's disease. The average spinal cell count is 200 to 500; there is an increase in the albumin and globulin fractions. The organism is best seen in India ink preparations. The authors feel that the bases of the lungs are most often infected. Roentgenograms in the early stage reveal small circumscribed areas of consolidation with only a small amount of reaction about their edges. There is a tendency to confluency and very little evidence of lymphatic drainage. Hilar adenopathy is not a prominent finding. While the pulmonary lesions closely resemble tuberculosis, more frequent involvement of the nervous system suggests a diagnosis of torulosis.

Three of the 4 reported cases died. The one surviving case was treated by chemotherapy, including sulfadiazine, penicillin, potassium iodide, and gentian violet, and also received deep roentgen therapy. No conclusions as to the best method of treatment are presented.

The article provides an excellent summary of torulosis and should be read in full to be appreciated.—*Robert C. Pendergrass, M.D.*

JAMISON, HORACE W., and CARTER, RAY A. The roentgen findings in early coccidioidomycosis. *Radiology*, April, 1947, *48*, 323–332.

Coccidioidomycosis may be acquired by no more exposure than that incidental to passing through an area of endemic infection. These areas include large sections of the arid Southwest, having in common long, hot, dry and dusty summers. A definite correlation has been established between the number and severity of dust storms and the incidence of coccidioidal infections in these regions. The disease is acquired by inhalation of dust contaminated with chlamydospores of the fungus, *Coccidioides immitis*.

An intradermal coccidioidin skin test with a 1/100 concentration of potent extract, if negative, will generally rule out the disease in all but a few of the more severe disseminated infections. The diagnosis is established with certainty by positive precipitin or complement-fixation tests, which are found only in the presence of active infection. Final proof is obtained by culture of sputum or guinea pig inoculation, with demonstration of the causative organism.

Clinically, the conditions most likely to be confused with acute primary coccidioidomycosis are influenza and primary atypical pneumonia. The patient complains of backache, headache, or general aching, or marked weakness, slightly sore throat, loss of appetite, and various indefinite gastrointestinal disturbances. Cough is nearly always present with temperature of a spiking type. Eosinophilia of 3 to 15 per cent is frequently encountered and, when present, is a helpful diagnostic sign. One striking feature in differentiating coccidioidomycosis from the commoner respiratory conditions is the occurrence of chest pain in a high percentage of patients.

One or two weeks later, painful nodules may develop on the shins and elsewhere, characteristic of erythema nodosum. In other cases, macular, papular, or vesicular lesions of erythema multiforme may appear. Skin lesions of these types, when associated with or following an acute respiratory infection, should at once arouse suspicion of coccidioidal infection.

A roentgenogram of the chest taken at the time of onset will show some degree of pulmonary infiltration in about 9 out of 10 cases. Infiltrations vary in extent from the slightest fuzzy thickening of hilar shadows to extensive consolidations occupying a major portion of the lung field. The infiltrations are mostly unilateral, homogeneous, usually hilar or basal in location, and show little tendency to lobar distribution. They vary in density from the lightest veil-like haze to consolidations approaching, but rarely equaling, the opacity of lobar pneumonia. As a rule, they are more uniform, less patchy, more circumscribed than the usual bacterial bronchopneumonias.

The appearance is most likely to suggest the findings encountered in primary atypical pneumonia. It is not often possible, on the basis of roentgenograms alone, to differentiate the two conditions.

Pleural effusion is encountered in approximately one-fifth of all acute primary cases but ordinarily is so small in amount as scarcely to fill the costrophrenic angle; it resolves rapidly and completely as a rule.

Roentgenologically, most coccidioidal cavities are so characteristic that they are seldom confused with other conditions when occurring in endemic areas. A solitary thin-walled ring-like shadow without surrounding infiltration is

typical. Cavities are occasionally encountered with walls so thin and sharply defined as to closely simulate congenital cysts. The differentiation from tuberculosis in the case of apical cavities, and especially those which are occasionally surrounded by coccidioidal pneumonitis, is often not roentgenographically possible. Certain other mycotic infections may produce lesions closely resembling those of coccidioidomycosis, roentgenographically.

Residual "burned-out" nodular or cyst-like foci of coccidioidomycosis are quite characteristic in roentgen appearance and are seldom confused with other conditions when occurring in endemic areas. Among diseases to be differentiated are primary tuberculosis, metastatic carcinoma, congenital cyst, adult tuberculosis, lung abscess, pyogenic and mycotic infections. The discrepancy between the clinical and roentgen findings is often helpful in establishing the diagnosis.

Cases in which mediastinal adenopathy is dominant are usually among the more severe and prolonged of infections and give rise to most of the fatalities. Among the conditions to be considered in the differential diagnosis are Hodgkin's disease, pulmonary tuberculosis, sarcoidosis and bronchiogenic carcinoma.—*Stephen K. Tager, M.D.*

HOLLINGSWORTH, R. K. Bronchiogenic carcinoma; an analysis of 343 cases. *Ann. Int. Med.*, March, 1947, *26*, 377–385.

A large factor responsible for the small percentage of operable cases of bronchiogenic carcinoma at the time that definite therapy must be decided upon is the period of delay that occurs between the onset of symptoms and the institution of treatment. This delay period is divided into two phases and an unnecessary prolongation of either may forfeit the patient's chance of cure. The first is between the onset of symptoms and medical consultation and the second is that between the first medical consultation and a positive diagnosis. With this thought in mind, the author reviews a series of 343 cases of pulmonary carcinoma from the various services of the University of Michigan Hospital during the period of January 1, 1938 to January 1, 1944. An attempt is made to bring to light clinical data which will aid in reducing these periods of delay and therefore increase the percentage of operability.

Sufficient data are present in the literature to show that there has been both a relative and absolute increase in the incidence of bronchiogenic carcinoma. The great majority of cases occurs in males between the ages of forty to sixty years. Operability, however, is not affected per se by age. The present series adds nothing to the various theories of etiology, but tends to confirm some of those generally accepted.

The author's conception of the pathology of bronchiogenic carcinoma has changed considerably in the past decade largely due to the availability of resected specimens of earlier lesions. Significant is the fact that the right lung is more frequently involved than the left. The lesions are roughly divided into two groups: those that arise in the hilar areas and those that originate in the lung periphery. Spread is by direct extension and by lymphogenous and hematogenous metastases. The regional nodes are more frequently the site of metastases. Next in frequency is spread to one or both lungs, either directly or by metastases. Other sites of metastases are the pleura, liver, brain, and one or more bones. Metastases and direct spread greatly influence operability.

A histopathological grouping is given which consists of (1) squamous cell, (2) adenocarcinoma (gland cell type), (3) undifferentiated (small cell type, round cell type, and the oat cell type). All are graded from 1 to 4 when possible. The bronchial adenomas classified as carcinoma, grade 1, are excluded from this study. The squamous cell type offered the best prognosis. Adenocarcinoma was found more frequently in women. Bronchial adenomas are likewise more commonly found in women.

Although the author was unable to determine the time lag between the first symptom and medical consultation in his series, he offers Overholt's figure of three or more months. However, in more than 50 per cent of the cases, a diagnosis of bronchiogenic carcinoma was not made for six or more months after the patient sought medical advice. As the initial symptom may be trivial, a low threshold of suspicion is important. The most frequent early symptoms are listed as cough, pneumonia, "flu," cold, chest pain, hemoptysis, dyspnea, and ease of fatigue. Cough in any form is stressed as the most important and initial complaint and the one most frequently explained away for one reason or another. The diagnosis of tuberculosis in the face of repeated negative sputum examinations oft times accounts for loss of much

valuable time. Other easy pitfalls must likewise be guarded against.

Diagnostic measures and points are reviewed in moderate detail. The problem of differentiating tuberculosis, bronchiectasis, and lung abscess is stated. Punch or aspiration biopsy is not recommended. In the presence of suspicious roentgen findings and repeated failure to establish a positive diagnosis, thoracotomy is stressed as a necessity. The hazard of lost time far exceeds the slight operable risk of this procedure.

Surgery is stated as the procedure of choice for treatment, and pneumonectomy is preferred to lobectomy. Roentgen therapy, except for palliation, is condemned.—*Robert N. Byrne, M.D.*

HEUBLEIN, GILBERT W., and GILFILLAN, CLARENCE D. N. A practical technic for visualization of the bronchial tree. *Radiology*, January, 1947, *48*, 37–44.

Bronchography as a diagnostic measure is often indicated when any of the following conditions is suspected: bronchial obstruction, mural growth, pulmonary neoplasm, atelectasis, recurrent bronchopneumonia, a chronic suppurative process. The procedure is definitely contraindicated in the presence of acute inflammatory disease of the tracheobronchial tree. It should be deferred in patients with acute upper respiratory infection and should be used with hesitation in those suffering from asthma.

Postural drainage, mild sedation and omission of atropine are suggested prior to the study. After gaining the patient's confidence by explanation of what is to follow, the pharyngeal region is anesthetized with 2 per cent pontocaine. Using indirect laryngoscopy, the vocal cords are anesthetized and 2 cc. is injected directly into the trachea. A flexible No. 14 catheter is inserted through the nose to a point just above the carina and checked by fluoroscopy in the upright position.

Positions to be assumed to fill the different segments are fully discussed. In general, a thorough appreciation of the anatomy of the bronchial tree in all planes is the basis for positioning for study of each pulmonary segment.

Untoward reactions due to surface anesthesia have been avoided by use of pontocaine. Treatment of severe pontocaine reactions could be remedied by oxygen inhalation and adequate intravenous barbiturates.—*Eugene J. McDonald, M.D.*

LAM, CONRAD R. Pericardial celomic cysts. *Radiology*, March, 1947, *48*, 239–243.

Congenital cysts of the mediastinum may be epidermoid, dermoid, teratoid, bronchial, esophageal, gastroenteric, pericardial celomic and cystic lymphangioma. The last two are purely mesodermal in origin but present striking gross and microscopic differences.

Cystic lymphangiomas are multilocular, cyst walls are of varying thickness, with a relatively complex histological structure. They are intimately attached to adjacent structures from which they derive their blood supply. They are difficult to remove and bleed severely.

Pericardial celomic cysts are simple in structure, unilocular, lined with thin layer of mesothelium. They are easily detached from surrounding parts. They contain clear or sanguineous fluid and are located adjacent to the pericardium. The latter arises from a series of disconnected lacunae which appear early in embryonic life which eventually fuse to form the pericardial celom. If one of these fails to merge it may persist to form a cyst in the vicinity of the pericardium.

Four such cases have been reported in the literature to which the author adds one of his own. A white female, aged thirty-nine, was admitted to the Henry Ford Hospital on March 12, 1944, with a chief complaint of low grade fever of ten years' duration, shortness of breath, fatigue and angina pectoris. For many years she was told she had heart disease, which interfered with her studies and work. In 1935 a chest film revealed unusual cardiac contour with a bulge in the upper left border, which was finally considered evidence of a congenital anomaly.

Periodic examinations showed continued cardiac enlargement which was more pronounced on expiration. Intermittent fever persisted. Anginal symptoms appeared in 1941. The first mitral sound was rough but without a true murmur. The heart became enlarged to the right and posteriorly but without visible pulsations at sites of enlargement. A tumor or cyst was considered the likely diagnosis.

On May 17, 1944, at operation a thin-walled cyst was found anterior to the heart and great vessels, extending to the right and posteriorly. One liter of clear fluid was obtained and then the cyst was easily removed. This was a simple cyst. Postoperative chest film showed normal cardiac contour with absence of the previous

shadow. The patient feels exceptionally well although recurrent fever persists.

The marked change in the contour of the mass between the two phases of respiration may well be a pathognomonic sign of pericardial celomic cyst at this location.—*William H. Shehadi, M.D.*

Sosman, Merrill C. Venous catheterization of the heart. I. Indications, technics, and errors. *Radiology*, May, 1947, *48*, 441–450.

Catheterization of the right heart is most useful in the study of hemodynamics, both in establishing the normals for physiological variations and the changes in the varied forms of heart failure, cardiopulmonary disease and shock. It is valuable also in helping to establish the diagnosis more accurately in congenital heart disease. This latter is especially important now, with the tremendous advances in curative cardiac surgery.

A single lumen catheter, size 9 French, of woven silk and radiopaque, is used. It is 100–125 cm. in length, flexible, and yet stiff enough so that it may be rotated by twisting the exposed end without buckling.

The catheter is threaded into either the right or left median basilic vein, advanced under fluoroscopic guidance and aimed at the desired area by pushing and twisting the proximal end. It is passed upward into the axillary vein to the superior vena cava and into the right auricle. If the tip is turned medially in the right auricle, it may be passed through the tricuspid valve into the right ventricle. From the right ventricle, it may be introduced through the pulmonary valve into the pulmonary artery.

Clotting of blood in the catheter is prevented by a continuous perfusion of normal saline. The comfort of the patient is important for the success of the test. Sedation may be used in nervous or apprehensive individuals.

In the author's series, only 13 out of 100 examinations were unsatisfactory. Venospasm around the catheter in the arm accounted for 2 of these cases. Ventricular extrasystoles occurred in about one-half of the cases when the catheter was passed through the tricuspid valve. This was the only subjective sensation in the great majority of patients. The dangers most commonly feared are damage to the endothelium of the large veins or of the heart, and the possibility of thrombus formation in or on the catheter. Several of the author's patients have succumbed to the disease or conditions not in any way related to the procedure, and in 10 autopsies, no trace of damage could be found in the lining endothelium of the superior vena cava, the right auricle, the right ventricle, the pulmonary arteries, or on the valves.—*Eugene J. McDonald, M.D.*

Dexter, Lewis. Venous catheterization of the heart. II. Results, interpretations, and value. *Radiology*, May, 1947, *48*, 451–462.

To obtain interpretable results in congenital heart disease, venous catheterization must be performed by a well trained team of at least three persons working smoothly and efficiently and should be used in conjunction with the usual procedures of history, physical examination, electrocardiography, fluoroscopy and, if available, the Robb-Steinberg technique of visualization of the cardiac chambers with diodrast. Findings in several representative types of congenital heart disease are described.

In auricular septal defect, blood usually flows from the left auricle to the right auricle. The venous catheter may be introduced through the defect or arterial blood may be found in the right auricle.

In uncomplicated defect in the interventricular septum, there is a shunting of arterial blood from the left ventricle to the right ventricle. Its recognition by venous catheterization depends on the finding of a significantly higher oxygen content of blood in the right ventricle than in the right auricle.

In the tetralogy of Fallot the following may be found: due to the pulmonic stenosis, venous blood enters the pulmonary artery with difficulty, and some is shunted through the septal defect and into the aorta. The venous catheter may follow one of two courses. It may pass through the stenosed pulmonary valve into the pulmonary artery, or it may pass through the interventricular septal defect and go directly into the overriding aorta.

In patent ductus arteriosus, there is a vascular anastomosis between the aorta and pulmonary artery, which during fetal life, serves to bypass the lungs. Its persistence after birth is deleterious, owing to the ease with which bacterial vegetations become implanted and also to the circulatory strain thrown on the left ventricle. The lesion is detectable on venous catheterization by finding arterial blood in the pulmonary artery or blood with a higher oxygen content than in the right ventricle.—*Eugene J. McDonald, M.D.*

HOLT, JOHN F. Epipericardial fat shadows in differential diagnosis. *Radiology*, May, 1947, *48*, 472–479.

It is common knowledge that epipericardial fat pads frequently are visible roentgenographically along the left heart border. However, not so widely recognized are large extra pericardial fat deposits adjacent to the right heart border. On the right side the fat pads are located between the pericardium and the pericardial pleura. Their shape is neither consistent nor entirely characteristic.

In frontal projection it most frequently assumes a triangular configuration, the outer margin of which is somewhat convex. In the lateral view the fat pad is located at the anterior costophrenic sulcus, and its smoothly marginated, bow-shaped, posterior border appears to fuse with the anterior chest wall.

A number of groups of patient case histories and roentgenograms are presented. One group of cases proved to have large right-sided epipericardial fat pads, and one interesting observation in one of these cases was that after a considerable weight loss the mass in the right costophrenic angle decreased in size. The other groups of patients were presented to illustrate the difficulty in differentiating these shadows from significant intrathoracic lesions.

Some of the lesions that produce similar shadows are neurofibrosarcoma, tracheobronchogenic cyst, subpleural tuberculoma, primary tuberculosis, cardiospasm, herniated gastric cardia, aneurysm, atelectasis, and so forth.

The author believes it inadvisable to attempt a roentgenologic diagnosis of a suspected fat pad on the basis of its appearance in a single posteroanterior projection, especially on a miniature film. He feels that a lateral view is very helpful in that significant lesions in the lower right lung field are more apt to be posterior in position, while fat pads are always anterior. He also suggests that complete gastrointestinal studies, bronchograms and bronchoscopy, and the passage of time are necessary means of establishing the differential diagnosis.—*F. B. Markunas, M.D.*

BATT, RICHARD C. A roentgenkymographic study of the heart in myasthenia gravis. *Radiology*, April, 1947, *48*, 374–380.

The roentgen kymograph is recognized as an instrument with ability to record permanently the motion of an organ observed fluoroscopically. Attention to certain variables which limit the use of the kymograph in studies of this type is recorded. Four normal persons and 16 patients with myasthenia gravis were examined at the Myasthenia Gravis Clinic of the Massachusetts General Hospital.

If the patient had been receiving prostigmine, the drug was withdrawn for twelve or more hours before the examination. During this period symptoms of lassitude, general muscle weakness, ptosis, dysphagia, dysarthria, and other signs of myasthenia gravis usually developed. A roentgen kymogram of the heart was then made. If the initial film was satisfactory, 1.5 to 2.0 mg. of atropine sulfate was given intramuscularly. Fifteen minutes later a second roentgen kymogram was obtained.

Patients with myasthenia gravis frequently showed a slightly increased chest diameter or a slightly lower diaphragm at deep inspiration after a prostigmine injection. This observation was confirmed teleroentgenographically and is consistent with the general picture of myasthenia gravis.

Of the 15 patients with myasthenia gravis, 10 showed a slight decrease in heart rate after the injection of prostigmine. The normal subjects showed a similar decrease after the same medication.

The cases in this series showed no remarkable changes in the waves of the aortic and auricular areas except for slight slowing of the rate. Very definite changes, however, were observed in the ventricular waves. In cardiac roentgen kymograms of patients with myasthenia gravis, spike-like configuration of waves along the ventricular border are noted.

After the prostigmine test dose, the heart rate becomes slower. The spiking of the left ventricular waves disappears. The diastolic limbs are smoother and have changed from concave to convex. Changes of this type were observed in 7 of the 15 cases studied.

It must be concluded that there is no cardiac roentgen kymographic wave form characteristic of this disease.

Limitations of the roentgen kymographic method are particularly noticeable when the auricular and aortic areas are examined. The waves in these areas are extremely variable, deceptive, and frequently difficult to interpret. In the average kymogram these particular waves often do not exceed 1.0 mm. in amplitude, rarely more than 3.0 mm. The superimposed vertebrae and mediastinal structures frequently obscure wave detail. Motion in any portion of

the cardiac border is the result of several directional forces and does not represent the true intrinsic pulsation of one chamber. Auricular waves frequently appear blurred and are often complicated by the distorting effect of transmitted ventricular pulsations. Aortic waves, although more distinct than auricular waves, are determined and influenced by such components as thrusts of blood from the left ventricle, contraction of the aortic wall, aortic tortuosity, and the effects of other stationary and moving mediastinal structures.

The prostigmine test dose produces no characteristic cardiac kymographic wave changes either in myasthenia gravis patients or in normal subjects. The test dose may slow the cardiac rate somewhat, thereby producing deceptive changes in wave contour.—*Stephen N. Tager, M.D.*

Clark, Stanley B., and Koenig, Edward C. Aortic aneurysm secondary to coarctation. *Radiology*, April, 1947, *48*, 392–397.

Clark and Koenig present 2 cases of calcified aortic aneurysm distal to the site of a coarctation. One case, occurring in a twenty-five year old diabetic woman, presented absence of the aortic knob, rib notching and multiple calcified ring-like shadows in the region of the descending aorta. This case was proved at autopsy when marked dilatation of the intercostal arteries was also demonstrated. A second case, not autopsied, showed absence of the aortic knob, multiple rib notchings and a soft tissue density distal to the aortic arch.

The article includes an excellent discussion of the routes by which blood may reach the aorta below a coarctation, namely collateral channels through (1) the scapular and cervical arteries, (2) the internal mammary, (3) the intercostal arteries, and (4) the spinal arteries. The authors conclude that the majority of aneurysms distal to the stenosis are formed directly as a result of the collateral circulation secondary to the coarctation, and are not related to infection.—*Robert C. Pendergrass, M.D.*

O'Loughlin, Bernard J. A study of 24,615 separation chest roentgenograms. *Radiology*, April, 1947, *48*, 389–391.

O'Loughlin reviews 24,615 chest films made upon separation from the Army Air Forces. The incidence of pulmonary tuberculosis was 0.1 per cent in this series of discharge films, compared with an average of 1.0 per cent in induction examinations. The incidence of other abnormalities was practically identical with that found on previous surveys. It was notable that 14 by 17 inch films were included in this survey rather than the smaller types of films. No definite conclusions could be drawn as to whether the 0.1 per cent tuberculosis originated during military service.—*Robert C. Pendergrass, M.D.*

Epstein, Bernard S. Rheumatic mitral valve disease without cardiac enlargement. *Radiology*, March, 1947, *48*, 249–255.

Roentgen studies are frequently sought in the diagnosis of mitral valve disease, demonstrating changes in cardiac size and contour. The accepted teaching is that teleroentgen studies reveal prominence of the second cardiac arc, due to prominence of the pulmonary artery and appearance of the conus arteriosus of the right ventricle on the left cardiac border. In the right anterior oblique position posterior displacement of the barium-filled esophagus indicates left atrial dilation. In the diagnosis of mitral valve disease left atrial dilatation is considered by some as next in importance to the pathognomonic apical diastolic murmur.

Twenty-five cases are reported, 17 females and 8 males, aged ten to sixty-three. Twenty had positive history of rheumatic fever, 2 of chorea, and 3 had no known rheumatic infection. Murmurs in all these cases were diagnostic of mitral valve disease. Blood pressure was within normal limits; the electrocardiogram, with one exception, was negative. Congestive failure occurred in one case during last months of pregnancy. Teleroentgenography and roentgenoscopy, including barium studies of the esophagus, was done. Heart contour and measurements were normal in all cases. The absence of heart failure supports the observation that the heart fails rarely if normal in size.

In the presence of characteristic apical murmur the diagnosis of mitral valve disease should be maintained despite absence of roentgen evidence of enlargement or alteration of cardiac contour.—*William H. Shehadi, M.D.*

Ungerleider, Harry E. Cardiac enlargement. *Radiology*, February, 1947, *48*, 129–142.

This article bears reading and re-reading. It is an extremely important contribution which contains a wealth of information concerning the normal and enlarged heart.

The article is primarily concerned with car-

diac measurements. That measurements are of greater value as an index of generalized enlargement of the heart rather than in determining the size of individual chambers is immediately pointed out by the author.

The author agrees that careful mensuration is unnecessary when gross enlargement of the heart exists. It is the lesser degrees of enlargement, however, that often escape detection unless careful measurements are resorted to. Conversely, apparently large cardiac shadows may assume less significance when considered in relation to standards of body build.

The author prefers to make most of his measurements from the frontal cardiac silhouette. The importance of a meticulous roentgen technique with the patient in the erect or sitting position and with respiration suspended in ordinary inspiration is stressed.

The author has correlated the size of the heart with various factors such as weight, height, surface area, muscular development, thoracic circumference and other thoracic measurements. Body build has a most important determining influence on the size of the heart. The dependence on weight is somewhat greater than on height but the correlation is improved if both weight and height are considered. Apparently, the influence of sex or age in adults on the size of the heart may be disregarded in prediction standards.

According to the author, the simplest and one of the most useful measurements is the transverse diameter which is the sum of the greatest extension of the right border of the heart and of the left border of the heart from the midline. In the author's opinion, the cardiothoracic ratio is crude and inexact.

Because of the increasing employment of teleroentgenograms of the chest for determining cardiac size, the author has developed a new prediction table based upon normal teleroentgenograms of 1,460 normal subjects. The actual transverse diameter of the heart should not be interpreted too strictly because of appreciable physiological variations in the size of the cardiac silhouette attributable to different phases of the cardiac cycle and to respiration. However, diameters more than 10 per cent above the predicted value may be regarded as abnormal and the heart may be considered as almost certainly enlarged if the transverse diameter is 15 per cent in excess of the predicted dimensions. The author discusses two other diameters, the long and broad diameters, which he considers somewhat less valuable than the transverse diameter. The long diameter extends from the junction of the cardiac and vascular silhouette on the upper part of the right border of the heart obliquely downward to the apex on the left. This diameter which is approximately 10 per cent greater than the transverse diameter is increased chiefly as the result of left ventricular enlargement. The broad diameter is the greatest diameter perpendicular to the long diameter. Whereas the broad diameter is often drawn as the sum of the two perpendiculars from the long diameter to the lower right and upper left heart borders, it more properly should be considered the greatest single diameter from upper left to lower right heart border perpendicular to the long diameter. The long and broad diameters are of interest not so much by themselves but for their product which represents the frontal cardiac area. Based upon these studies the author recently prepared a nomogram for prediction of the cardiac area from weight and height and actual area as calculated from the long and broad diameters.

It is the author's opinion that the use of either or both the transverse diameter and the nomographic determination of frontal area presents two simple and accurate methods which should suffice to determine whether cardiac enlargement is present.

The author also found that the transverse aortic diameter in normal subjects is closely related to weight and height. Based upon these studies a table was established for predicting the transverse diameter of the heart from weight and height which seems very reliable. It is noteworthy that the right border of the vascular pedicle is formed on the superior vena cava in the majority of young subjects whereas in later life it is more frequently formed by the right border of the ascending aorta.

The author suggests that interpretation of heart size should not be confined to measurements alone. He urges that, as far as possible, enlargement should be described in terms of the chambers involved since characteristic changes occur in various types of heart disease.

This article contains a complete table of theoretical transverse diameters of the heart for various heights and weights.—*Philip J. Hodes, M.D.*

ABDOMEN

GERSHON-COHEN, JACOB. A duodenal mechanism regulating the motor and secretory activity of the stomach; its roentgenographic disturbance in duodenal ulcer. *Radiology*, March, 1947, *48*, 232–238.

The duodenum contains a mechanism influencing tone, peristalsis, pyloric action and gastric secretion. In duodenal ulcer this mechanism is disturbed resulting in abnormal motor and secretory function.

Normally a 250 cc. barium-water meal leaves the stomach in about sixty minutes. Adding 0.25 per cent HCl to the meal delays gastric emptying. When 0.25 per cent HCl solution is dripped into the duodenum emptying is still more delayed, while isotonic alkaline solutions have no effect. Stronger acid and alkaline solutions, hypertonic solutions of electrolytes or non-electrolytes cause marked delay. Fats and fatty acids are most powerful stimulants of the duodenal mechanism, hence their importance in ulcer therapy. With stimulation of the duodenal mechanism gastric peristalsis abates, the pylorus contracts and emptying is delayed or stopped. The duodenal bulb is most sensitive to such stimulation. In duodenal ulcers, which occur mostly in the bulb, normal stimuli are inadequate to stimulate the inflamed mucosa, hence disturbed motor function and rapid emptying.

In healing of a duodenal ulcer normal sensitivity is recovered by the duodenum with disappearance of gastric motor and secretory disturbances. Persistence of the latter after disappearance of the ulcer crater and symptoms should make the roentgenologist cautious in evaluating healing.—*William H. Shehadi, M.D.*

OULD, CARLTON L., and DAILEY, MORRIS E. Simultaneous radiographic and gastroscopic examination of the stomach. *Radiology*, January, 1947, *48*, 8–14.

In an attempt to clarify differences in the roentgenographic and gastroscopic appearance of the stomach, the authors made simultaneous roentgenographic and gastroscopic examinations of the stomach in 4 patients. In order to visualize the mucosa, a medium had to be found which would give satisfactory contrast on the films, yet be relatively transparent at gastroscopy. The high cost of a very excellent medium (pantopaque) prevented its routine use. The medium finally selected by the writers for their studies was composed of equal parts of diodrast and a saturated aqueous solution of methyl cellulose.

Using the stomach of a fresh cadaver, distended and inflated without distortion on rubber strips between parallel metal bars, it was found on gastroscopic examinations that the fundus, the lesser curvature between the angularis and pylorus, as well as a strip of the posterior wall were in blind areas. Immediately after emptying the stomach, 60 cc. of the methyl cellulose-diodrast mixture was instilled and the gastroscope was promptly inserted while the patient was lying on his left side on the roentgenographic table. By this method a sharp round image of the mucosa was obtained, and vision was clear at any angulation as long as the flexible portion of the gastroscope deviated no more than 30° from the long axis. Roentgenograms were taken in the left lateral and anteroposterior projections, recording the position of the gastroscope at the moment the gastroscopist visualized important landmarks in the stomach. As much as 2,000 cc. of air may be introduced into the stomach during the course of a routine gastroscopy. Films demonstrated that there was a considerable amount of air distending not only the stomach but the duodenum and upper small intestine as well. This surprising amount of air in the small intestine, increasing in volume as the examination progresses, pushes the stomach anteriorly and may in some instances distort its lower pole considerably. Even with the little weight of the medium used the stomach was seen to pass well across the spine to the left or lowermost side of the body. This extensive mobility may well be significantly reduced in cases where perigastric inflammatory or neoplastic infiltration and adhesions have fixed the stomach. Roentgenologic studies might prove this to be a differential point of importance, for it is known, for instance that when the pylorus is seen abnormally far posteriorly on gastroscopy, the presence of a penetrating duodenal ulcer is suggested. This method would have real clinical value if, thereby, radiologists could inform surgeons that a pathologic process had extended beyond the stomach.

This study suggests that the zones visualizable at gastroscopy could be increased by a slight change in the instrument. If the source of light were not separated from the objective,

the angulation and the cone of light would more nicely coincide. This would make it possible to see more of the posterior wall.—*Samuel G. Henderson, M.D.*

ZANCA, PETER. Gastrocolic fistula complicating carcinoma of the colon; a case report. *Radiology*, March, 1947, *48*, 244–248.

Gastrocolic fistula, a long established entity, is rare. It occurs as a complication of other gastrointestinal or intra-abdominal lesions. The clinical diagnosis can be made in the presence of fecal vomiting without intestinal obstruction. Other symptoms are fecal odor to the breath, general weakness, extreme weight loss, persistent diarrhea with undigested food in stools. Signs and symptoms may vary with different lesions. Roentgen studies readily establish the diagnosis.

A thirty-seven year old male was admitted to the hospital because of rectal bleeding, abdominal pain, diarrhea, general weakness and a left upper abdominal mass. Patient consumed a pint of whisky daily. He was discharged from the Army because of varicose veins. Symptomatic treatment seemed to relieve several attacks of cramps and abdominal pain seven months prior to admission.

Laboratory studies revealed marked anemia, negative Kahn reaction and urinalysis. Gastric total acidity 130 and free HCl 110 (after histamine). Stool, occult blood three plus.

Roentgen studies: Chest negative. Esophagus normal. Barium demonstrated an irregular filling defect of the greater curvature, and passed immediately into the descending colon. Barium enema demonstrated a filling defect in the region of splenic colon then entered the stomach through a fistulous tract, which was best visualized after air injection. A palpable mass was present at this level.

The tumor was resected and a gastroenterostomy and an end-to-end anastomosis of the colon performed. The tumor was a primary carcinoma of the distal transverse and splenic colon, with involvement of the greater curvature of the stomach. The fistulous tract was lined with tumor tissue.

Microscopic diagnosis was adenocarcinoma of the colon.

Following a mildly stormy course the patient made an excellent recovery, has gained weight, is up and around and active two months after operation.—*William H. Shehadi, M.D.*

EUPHRAT, EDWIN J. Roentgen features of mucocele of the appendix. *Radiology*, February, 1947, *48*, 113–117.

The author reports his findings in a patient with mucocele of the appendix in which the correct preoperative diagnosis was made on the basis of criteria previously reported by Åkerlund.

According to Åkerlund, fairly definite roentgen criteria for this diagnosis have been established. Usually a sharply circumscribed globular or reniform soft tissue mass with considerable mobility firmly attached to the cecum is found. As a rule, the cecum is displaced medially by this mass. Finally, the presence of *calcium deposits* in the wall or substance of the mass, particularly when the appendix has not been visualized, is of particular significance.

Reviewing the literature, the author found that mucoceles of the appendix occur approximately once in every 300 operated upon. It is generally accepted that the primary etiologic factor is obstruction of the lumen of the appendix in the absence of pyogenic infection. The lesion is usually benign. When the cyst contains an adenocarcinoma which ruptures into the peritoneal cavity, pseudomyxoma peritonei may result. Usually the lesion varies in size from a small localized enlargement of the appendix to a globular mass which may be more than 10 cm. in diameter.

This article contains excellent photographs of a mucocele of the appendix which had been removed surgically, with reproductions of the original barium enema films which clearly visualize the defect produced by the small tumor mass in the right lower abdominal quadrant.—*Philip J. Hodes, M.D.*

BREWER, ARTHUR A. Cholecystography: a comparative study of oral and intravenous contrast substances. *Radiology*, March, 1947, *48*, 269–273.

Of 150 patients examined with priodax, 104 showed normal gallbladder shadows; the other 46 cases were studied by intravenous sodium tetraiodophenolphthalein in addition to priodax.

The results were similar in 39 of the two examination studies and dissimilar in 7 of the cases. The disagreement arose when the priodax examined cases yielded faint shadows and on intravenous examination were found to have

normal concentration. Some of these patients later showed normal priodax concentration.

The author feels that the faint priodax shadow may be due to organic pathology or to physiological stasis of bile which may be eliminated by adoption of a routine high fat diet immediately prior to priodax cholecystography.—*Samuel H. Fisher, M.D.*

Rigler, Leo G., and Mixer, Harry W. Cholangiography and biliary regurgitation. *Radiology*, May, 1947, *48*, 463–471.

Opaque oil was discontinued because of viscosity and its tendency to form globules which result in uneven distribution. Thorium dioxide sol was used until some leaked into the peritoneal space and caused a violent peritonitis. Now diodrast is used. With this solution a partial or complete obstruction to the common ducts sometimes gives a visualization of the kidney pelves. However, at other times the kidney pelves do not show even though obstruction of the common duct exists. This is explained as due to lack of sufficient pressure upon the opaque material to cause a regurgitation from the biliary radicles into the blood stream. The visualization of the kidney pelves was observed in 8 cases out of 460 cholangiographic studies.

The cause of systemic reaction following the procedure is discussed. The opinion is advanced that such reactions are due to transient bacteriemia rather than to distention of the bile ducts. Therefore, care should be exercised to keep the injection pressure low enough to avoid forcing bacteria or other foreign material into the blood stream.—*J. H. Harris, M.D.*

GYNECOLOGY AND OBSTETRICS

Scarpellino, Louis A. Cephalopelvimetry. *Radiology*, January, 1947, *48*, 45–49.

One of the factors contributing to the difficulty of labor is the size and weight of the fetus. Unquestionably, weight and size are to be considered, but if the head of an apparently normal fetus can be delivered, the act of parturition can be consummated. From a clinical-obstetrical, as well as a roentgen-mensuration standpoint, cephalopelvimetry resolves itself into two main procedures: determination of the capacity of the maternal pelvis, and determination of the size of the head that must be delivered.

The method proposed by Ball and Marchbanks in which the linear measurements of a maternal pelvis and the circumference of the fetal skull can be expressed in terms of volume, represents a decided advance. In most methods of cephalometry, attempts are made to measure the lineal diameter of the fetal skull, but there is no assurance that the particular linear diameter measured represents the dimension that is to be delivered. Also because of rotation and position of the fetal head, this linear measurement is difficult to attain accurately, and is unquestionably subject to considerable error. If the circumferences of a spheroid are taken at right angles, the volume determined from their mean average will approach the volumn of a sphere having the same perimeter measurements. Practically, therefore, the fetal head may be considered a sphere.

According to Ball's technique, the symphysis pubis is the fixed point from which all measurements in the mid-sagittal plane of the body are made. In the author's experience, when the symphysis and sacrum do not coincide, the error relative to the fetal head volume is considerable. To reduce the error of magnification, the difference between the ventral and dorsal mid-sagittal planes is bisected to arrive at the object-film distance for the lateral circumference of the fetal head. In the case of breech presentation the posteroanterior standing projection is used, together with a right or left lateral projection, depending on the position of the fetal head relative to the mother. By this technique, the fetal head is closer to the film, easier to delineate, and subject to less distortion. The difficulty and duration of labor increase as the disproportion between the fetal head and the smallest plane of the pelvis approaches 200 cc. in the anterior, and 135 cc. in the posterior rotation. The author has studied 500 cases at various intervals during pregnancy, and obtained the head measurements. His figures show an average error of ± 10 cc. in volume or ± 2 mm. in circumference. A corrected growth curve is presented, showing the absolute volume of the fetal head in utero, on the basis of this series.—*Eugene J. McDonald, M.D.*

GENITOURINARY SYSTEM

Myers, Leonard A. The range of usefulness of intravenous pyelography. *Radiology*, January, 1947, *48*, 63–65.

In patients suspected of sensitivity, the author gives a trial injection of 3.0 to 5.0 cc.

intravenously and completes the injection after a five minute interval. Over 1,500 examinations were made in ten years, and all injections of the dye were completed. No deaths were attributable to the procedure.

Concentration of the urine by dehydration of the patient has been found more effective than the use of large amounts of dye.

In children, the period of maximum concentration is at the five minute interval. In adults up to fifty years of age, maximum concentration is found at about fifteen minutes, while in the aged, it is usually later.

Pathological alterations in clearance are of three types: (1) acute mechanical suppression, when the renal parenchyma shows considerably more concentration than does the unobstructed kidney. There is no associated cortical thinning of the affected side, nor any compensatory hypertrophy of the unaffected kidney; (2) chronic mechanical obstruction may show that the functional thrust of the affected kidney is delayed for one or more hours, and there will be more or less cortical thinning associated with varying degrees of pelvic dilatation. There will also be found compensatory hypertrophy of the cortex of the opposite kidney as well as compensatory function; (3) in nephritic involvement without mechanical obstructive uropathy there is poor concentration on both sides throughout a long period of clearance without ureteral pelvic distention.

Bilateral ureteral compression is made over the sacroiliac areas at the period of maximum thrust, which is usually at the fifteen minute interval. Compression is maintained for five minutes at the end of which time the proximal half of each ureter and the pelvis and calyces of each kidney are filled to distention if no organic lesion is present. Lack of distensibility suggests pyelonephritis. Ureteral kinks and unusual excursion of the kidneys not producing a disturbance in drainage, are not considered pathological.—*Eugene J. McDonald, M.D.*

NERVOUS SYSTEM

SCOVILLE, WILLIAM B., MORETZ, WILLIAM H., and HANKINS, WALTER D. Discrepancies in myelography; statistical survey of 200 operative cases undergoing pantopaque myelography. *Surg., Gynec. & Obst.*, May, 1948, *86*, 559–564.

Many articles have extolled the virtues of pantopaque and other contrast myelography in the study of the ruptured intervertebral disk. The authors attempt to point out certain limitations of this diagnostic method. They have surveyed 200 operative cases from Cushing General Hospital in 1944–1945. The survey was undertaken when the neurosurgical author and several independent roentgenologists commented on the difficulty in making a clear cut diagnosis of the presence or absence of a ruptured disc by myelography alone.

From a detailed analysis of these 200 cases it appears that the largest percentage of error occurs in those myelograms incorrectly diagnosed as normal. In fact, if operation is performed upon all cases having clinical evidence of a disc but a "normal" myelogram, an error in myelography will be found in 74 per cent of those cases. Twenty-four of 25 cases in this 74 per cent will reveal a laterally placed lumbosacral disc at operation. The second largest percentage of error occurs in the false localization of single discs. These two groups together cause 50 per cent of all myelographic errors. In contradistinction, technical errors are few and "positive" myelograms will be correct in 95 per cent of the cases. With these facts in mind the authors will continue to use pantopaque myelography routinely on all ruptured disc suspects but will tend to discount all "normal" myelograms if contradicted by the clinical findings.

Conclusions

1. Clinical evidence of a ruptured disc is more important than is myelographic evidence.
2. A positive myelogram is more important than a negative myelogram. A negative or normal myelogram in the face of clinical evidence of a ruptured disc will be wrong three out of four times.
3. Myelography fails to rule out the presence of a laterally placed lumbosacral "disc." In 24 of 25 cases of ruptured disc in which the myelograms are normal, the location is in the lateral lumbosacral interspace.
4. Root sheath asymmetry is an important yet equivocal myelographic sign which may or may not indicate the presence of a ruptured disc; it is of little value without confirmatory clinical evidence.
5. Myelographic double defects are more common than are actual double "disc" ruptures or herniations.
6. When myelography is used as the sole diagnostic criterion, the over-all error is in the neighborhood of 25 to 35 per cent in contrast

to the 6 to 8 per cent cited in the literature.—*Mary Frances Vastine, M.D.*

Denny-Brown, D. Primary sensory neuropathy with muscular changes associated with carcinoma. *J. Neurol., Neurosurg. & Psychiat.*, May, 1948, *11*, 73–87.

Two cases of primary simple degeneration of dorsal root ganglion cells associated with primary degeneration of muscle ("polymyositis") are described. Both cases presented a spreading numbness and sensory loss of the extremities and one of the face, without pain, but with severe and progressive ataxia. In both instances, bronchogenic carcinoma was present. Presence of a metabolic disorder related to the tumor cells is presumed, for the neuromuscular condition reproduced changes that have been seen in pantothenic acid and vitamin E deficiency in animals.—*Russell R. Jauernig, M.D.*

SKELETAL SYSTEM

Gilmore, John H., and Mahan, Thomas K. A case of acromegaly presenting specific roentgenographic changes. *Radiology*, January, 1947, *48*, 50–53.

Overgrowth of the lateral and anterior aspects of the bodies and intervertebral discs, resulting in a thickening of the spinal column, are described as specific changes in acromegaly. Erdheim is quoted as stating that he was able to distinguish between the original vertebral bodies which presented a biconcave configuration, and the additional bone proliferation which extended directly from their anterior and lateral aspects. Similar proliferation of the cartilage of the intervertebral discs was observed. Other authors are quoted who showed the autopsy findings of an acromegalic where pronounced fusiform widening of the ribs, and irregular ossification of the costochondral junctions were observed.

A case report of a white male, aged thirty-one, is presented, with costochondral and vertebral changes present as shown by roentgenograms.—*Eugene J. McDonald, M.D.*

Galluccio, Anthony C. Observations on gunshot fractures of the mandible. *Radiology*, March, 1947, *48*, 260–265.

More than 200 mandible fractures due to direct force (gunshot wounds in soldiers) are considered. Routine roentgenography consisted of right and left lateral oblique films and posteroanterior films all in stereo. Intraoral films were used as an adjunct.

Osteomyelitis was not a common complication; non-union was demonstrated by the usual methods. It was noted that clinical union preceded roentgenographic union by many months.

Most fractures seen were comminuted, located mostly in the anterior body and symphyseal regions. Twenty-two per cent of the cases had extensive bone loss, 25 per cent showed metallic foreign bodies and 38 per cent of the cases had associated facial bone injuries.—*Samuel H. Fisher, M.D.*

Cooper, George, Jr., Adair, Norman, and Patterson, William M. Familial osseous atrophy. *Radiology*, May, 1947, *48*, 509–513.

One case of familial osseous atrophy, a disease of unknown etiology, is reported in a white male, aged twenty-five. The patient's complaint began with pain in the feet on long periods of standing, especially at the first and second metatarsal heads where thick callus appeared. When the callus had been present several months it blistered and sloughed, leaving large ulcers. The ulcers recurred with sloughing of small pieces of bone until the distal ends of the feet were lost.

The roentgen findings are atrophy and necrosis of bone with multiple amorphous sequestra. No periosteal reaction. The cortex was moderately decreased in density and the surface slightly irregular. The authors demonstrate their findings in roentgenograms and state that they are characteristic of the disease.

In the family history it was found that the patient's paternal grandfather, father and two uncles suffered from the same condition until their feet were practically gone.

The disease is progressive after onset and terminates in crippling of the patient, but no deaths have been known to occur from this malady.—*F. B. Markunas. M.D.*

Russo, Peter E. Malignant melanoma in infancy. *Radiology*, January, 1947, *48*, 15–19.

Malignant tumors most frequently seen during the first five years of life are retinoblastomas, renal tumors (Wilms'), and neuroblastomas of the adrenals or sympathetic nervous system, usually in the order mentioned. Melanomas occur very infrequently but they may be present at birth or they make their appearance at any time during life. Many are first noticed

shortly after puberty. It is doubtful that a nevus first recognized later in life is of recent origin; it is probably due rather to growth of a previously quiescent lesion. Only a small percentage of melanomas ever become malignant.

In children the predisposing factor of trauma or irritation is insignificant, and hormonal stimulation has been suggested by some authorities as playing an etiologic role.

Three cases are reported by the author—1 being congenital and 2 occurring at the age of three years. In the child with a congenital lesion evidence of wide spread metastases was present at birth. Roentgenographic examination revealed destructive bone lesions involving the lateral aspects of the distal metaphyses of both femurs, with little evidence of bone reaction. In their symmetrical distribution and location, the lesions were not unlike those seen in congenital syphilis of bone. In an Indian girl aged three years a malignant growth was not suspected until microscopic examination of the tissues was done. In spite of early excision of the primary lesion only six weeks after the period of onset metastases had already taken place. Films of the skeleton revealed destructive lesions involving the 5th lumbar vertebra and the left sacroiliac joint, the sacrum, both iliac bones, the upper ends of the femurs, and the 9th dorsal vertebra.

In the third case, a three year old colored girl, a small nodule first became noticeable about one year before medical consultation. It was located on the lateral aspect of the left knee. The lesion was widely excised. A lymph node in the left inguinal region was noted soon after. Because of inability to determine definitely whether the enlarged inguinal node was of an inflammatory or malignant nature, a very moderate amount of deep roentgen therapy was given—1,200 r, in air (170 kv., 20 ma., 50 cm. distance, Thoraeus filter). The child was not seen again until three months later. The lymph node in the inguinal area had enlarged to twice its previous size. The involved lymph node was removed and ligation and section of the left saphenous vein was performed. Microscopic examination of the tissue showed invasion replacement with tumor cells resembling those occurring in the original lesion. Additional deep roentgen therapy over the left inguinal area was given, similar in amount to the previous series. This patient has been closely followed for over three years without any evidence of recurrence or metastasis.—*Samuel G. Henderson, M.D.*

ROENTGEN AND RADIUM THERAPY

McINDOE, A. H., FORBES, ROBERT, and WINDEYER, B. W. Symposium: radiation necrosis. *Brit. J. Radiol.*, July, 1947, *20*, 269–278.

A. H. McIndoe: Few radiologists know how common radiation necrosis is, because the patient often does not return to the radiologist after the development of this condition, and because the serious effects do not develop until much later. Ultimately they all see plastic surgeons. The great majority of these patients have been treated for benign conditions.

After repeated doses of roentgen radiation, and after the acute inflammation has subsided, pigmentation, telangiectasis, and progressive atrophy follow. Because of markedly reduced healing power eventual trauma followed by infection produces an ulcer which heals with difficulty. Malignancy develops in one-fifth of the cases.

The lesions which previously led most frequently to ulceration after roentgen-ray overtreatment are lupus, tuberculosis, exophthalmic goiter, superfluous hair, and psoriasis. These were usually in non-functional areas of skin, and plastic repair was accomplished fairly easily.

Most recently, the lesions, the treatment of which leads most frequently to ulceration, are plantar and palmar warts and pruritus ani and vulvae. Ulceration in these sites exposes important structures and repair is not so easy. In the hand, permanent crippling follows unless an efficient covering is rapidly supplied. In the foot, grafts are usually not successful and do not sustain weight-bearing well. In the perineum it may be necessary to do a colostomy or even a vulvectomy, and reconstruction is difficult.

McIndoe proposes that benign lesions of the palms, soles or perineum be treated by means other than roentgen radiation.

Robert Forbes: Fundamentally, roentgen treatment is the use of roentgen rays to produce partial or complete death of certain tissues that are superficial or deep. A justifiable degree of therapeutic necrosis is sometimes difficult to distinguish from an unjustifiable degree of radiation necrosis. In an

attempt to delineate the boundary between these two, it must be remembered that there is a patient-physician contract. The patient is obligated to pay for the treatment and the physician is obligated to furnish a requisite degree of care and skill such as might reasonably be expected from an individual of his qualifications and experience. If the physician uses this care and skill with the consent of the patient for the treatment it is quite unlikely that a court of law would find the physician negligent if a patient sustained damage by the treatment. On the other hand, radiation necrosis is an obvious condition which speaks for itself, and in defending himself against an allegation of negligence the radiologist must consider the safety of the dosage, the sensitivity of the patient, the adequate shielding of adjacent structures, and the follow-up of the patient. The radiologist is legally liable for the provision of safe equipment.

When a radiologist is confronted with an awkward situation relating to radiation necrosis it is wise for him not to attempt to handle the matter himself, but he should give it immediately to his medical defense organization.

B. W. Windeyer: Acute necrosis develops immediately after treatment. The erythema is followed by a fibrinous membrane on the mucosa or on skin by dry and then moist desquamation. Edema rapidly follows, the lesion is painful, and a slough of variable depth occurs. Endarteritis and fibrosis prevent healing for months or years. This type is caused by (1) overdosage of normal tissue, (2) overtreatment of sensitive areas, as the perineum, sole, palm, or a scar, (3) treatment of previously irradiated areas or (4) treatment in the face of acute bacterial invasion. It may even result from over enthusiastic nonradiotherapeutic treatment of a normal roentgen irradiation reaction.

Late necrosis occurs months or years after treatment which has caused fibrosis and local anemia. It may be obvious damage as in skin, or hidden damage, as in the bone and cartilage. The treatment may have been single and massive or multiple in suberythema doses. Ulceration is preceded by fibrosis and telangiectasis which lower resistance to physical and bacterial trauma and these, combined with poor blood supply, permit eventual ulceration. Late necrosis is sometimes easily confused with malignant ulceration in a recurrent lesion, and the two may coexist. Late necrosis of bone and cartilage deserve special mention because of the prolonged course and insidious development. Underlying cartilage and bone in the mouth, throat, chest, hand, foot, and scalp are particularly susceptible because of the frequency of trauma in these regions.

In another fashion necrosis may be divided into four types. First, it may be an inevitable risk in a perfectly justifiable attempt to cure cancer. Second, it may be unjustified as in faulty technique, ignorance of the effects of roentgen rays, and treatment of a necrotic ulcer mistaken for a recurrence. Third, it occurs in patients who are being treated palliatively. Since, in some, the best palliation is achieved by giving a curative dose, in some cases the ulceration is justified. Fourth, the majority of cases of necrosis occur in the treatment of nonmalignant conditions. Where it develops the dose was unjustifiably large, or an unsafe dose was given to a sensitive region, or repeated doses were mistakenly given.

Radiotherapy is usually safe in ringworm of the scalp, sycosis barbae, thyrotoxicosis and keloids. It should not be used in hypertrichosis, hyperidrosis, or pruritus ani. A carefully selected group of plantar and palmar warts might possibly be safely treated with a single dose of roentgen rays.

In the field of treatment of malignancy the development of some ulceration is inevitable and a therapist who has never seen a case develop after his treatment has been guilty of the greater crime of consistent inadequate dosage. —*E. F. Lang, M.D.*

Cross, James E., Guralnick, Eugene, and Daland, Ernest M. Carcinoma of the lip—a review of 563 case records of carcinoma of the lip at the Pondville Hospital. *Surg., Gynec. & Obst.*, Aug., 1948, *87*, 153–162.

Carcinoma of the lip, one of the most malignant neoplasms of the oral cavity, is one of the most readily curable malignancies encountered in the body. Because of the prominent location it is usually brought to the attention of the patient at an early stage and, therefore, should be seen by the physician while still amenable to treatment. This study was undertaken in an effort to evaluate the results of treatment of all patients with carcinoma of the lip either seen in the Out-Patient Clinic or admitted to the Pondville Hospital from the time of its establishment in June, 1927, to December, 1941.

This particular time period was chosen in order to have a complete five year follow-up record on all the patients who received treatment.

Conclusions

1. Carcinoma of the lip is the most readily curable malignant tumor of the oral cavity and treatment of 407 unselected cases at the Pondville Hospital resulted in 67.1 per cent three year cures. Of the patients who received all their treatment at Pondville 81.4 per cent achieved three year cure status.

2. Surgery is the preferred method of treatment at this hospital.

3. Three year cures are as significant statistically as five year cures in carcinoma of the lip.

4. Carcinomas of the labial commissures are approximately twice as difficult to control as lesions in other locations on the lips.

5. Curability of carcinoma of the lip is directly related to the size and pathological grade of the primary tumor and the presence (or absence) of lymph node metastases.

6. It was found that 35.9 per cent of the patients who underwent neck dissection, with pathologically proved cervical lymph node metastases, attained the three year cure stage. —*Mary Frances Vastine, M.D.*

RICHARDSON, W., and ROBBINS, L. L. The treatment of polycythemia vera by spray irradiation. *New England J. Med.*, Jan., 1948, *238*, 78–82.

Control of polycythemia vera by long bone irradiation was first reported by Lüdin in 1916, and in 1932 Sgalitzer described the results from total body irradiation. At the Massachusetts General Hospital, spray irradiation covering a field from neck to knees has proved the most successful of any procedure tried, although the authors point out that comparative results of radioactive isotope therapy were not studied.

Twenty-eight cases were treated, using anterior and posterior fields on alternate days. Factors of 200 kv., 0.5 mm. copper and 1.0 mm. aluminum filtration (half-value layer 0.92 mm. copper), were found satisfactory. The daily dose was 20 to 30 r, measured in air, and the total dose approximately 300 to 500 r in any one series, divided between anterior and posterior fields. Selection of a small daily dose seemed to prevent severe roentgen sickness, and prolonged remissions were obtained. The amount of treatment is determined by following the total white blood cell count. Treatment is stopped when the white count falls below 5,000. Red blood cell and hemoglobin levels are not considered, as there is apt to be little change in these values for one or two months.

Twelve patients died, the deaths in 4 apparently unrelated to the polycythemia or its treatment.

Thirteen of the 16 living patients have no symptoms attributable to polycythemia. One has persistent hypertension, a second has a refractory anemia possibly due to the irradiation, and a third has numerous symptoms and an increased red blood cell count although still alive after seven years. Tabulation of the duration of remission produced by single courses of from 200 to 1200 r suggest that a total dosage of 400 to 500 r may be expected to produce a remission of six months to five years.

Treatment of polycythemia vera by phlebotomy is condemned as unsound because of its stimulating effect on bone marrow activity, its production of "plethoric anemia," and its apparent propensity to result in leukemoid states. The use of phenylhydrazine has been discarded because of difficulty in regulating dosage.

Although effective and safe when properly used, spray therapy is dangerous if employed injudiciously. It is specifically contraindicated in elevated red blood cell count due to anoxia, in the occasional high red cell count of extramedullary hematopoiesis ("myeloid metaplasia"), and in the benign familial hypochromic polycythemia often seen in members of the Italian race.—*Henry P. Brean, M.D.*

POHLE, ERNST A., and TOMLINSON, CAROL. Roentgen therapy in traumatic myositis ossificans. *Am. J. M. Sc.*, April, 1948, *215*, 372–380.

Ten cases of symptomatic myositis ossificans traumatica are presented which were treated with roentgen rays.

Technical factors: 175 or 400 kv., 50 cm. focus skin distance, half-value layers of 1.05 mm. Cu and 2.4 mm. Cu respectively. Field size was large enough to include a wide zone about the area of calcification; doses of 150–200 r (air) are delivered to one to two fields daily or every other day for three or four treatments. When indicated, a second series is given in four to six weeks and a third in two to four months after the first series. In 5 cases, only one course was necessary.

Complete relief of pain was observed in all

cases. Limitation of motion was markedly improved or restored to normal in all but one, in which only slight improvement in function was made.—*Russell R. Jauernig, M.D.*

DEL REGATO, J. A. The role of transvaginal roentgen therapy in the treatment of carcinoma of the cervix. *Surg., Gynec. & Obst.*, April, 1948, *86*, 480–486.

In the majority of cases of carcinoma of the cervix, a thorough external irradiation is the most important single factor leading to permanent control. But the external irradiation is seldom sufficient to sterilize the tumor. The diminution of secondary infection and inflammation and the diminished dimensions of the tumor area, resulting from the external pelvic irradiation, make it possible for the internal phase of the treatment to achieve the destruction of the remnant of the tumor. The internal treatment compensates for the insufficient total dose and rather weak daily dose received by the remaining carcinomatous cells. A skillful application of radium in the uterus and in the vagina succeeds in controlling the residual tumor in an appreciable number of cases. The author has no quarrel with this classic form of treatment that could yet yield better results. The question is whether transvaginal roentgen therapy can achieve the same purposes with less disadvantages and whether or not it can improve upon the results of curie therapy of carcinoma of the cervix.

Following a course of external pelvic roentgen therapy lasting approximately six weeks, the author's patients receive a course of transvaginal irradiations without interval of rest. A single wide circular intravaginal field is used. This includes the cervix and fornices and permits irradiation of adjacent portions of the parametria. With the use of a single field, the dose that could be expected to be effective extends only partially into the parametria, but when transvaginal roentgen therapy has been preceded by external irradiation the area of combined effectiveness may extend as far as the pelvic wall.

All patients reported in this paper were treated with a 110 kilovolt unit at 25 centimeter target-cervix distance; at present the author is treating his patients with a 140 kv. unit and with 0.5 mm. copper filtration. In general, ten consecutive treatments of 400 roentgens, or a total of 4,000 roentgens in eleven days (measured in air at the level of the cervix) were given to the patients reported in this paper.

Conclusions. Transvaginal roentgen therapy is a valuable adjunct of external pelvic irradiation in the treatment of carcinoma of the cervix. It is the treatment of choice for carcinomas of the cervical stump. Lesser infectious and urinary complications, a low incidence of fistulas, and an apparent reduction in the proportion of local recurrences are the main advantages; in addition, this form of treatment does not require hospitalization. A three year symptom-free survival of 44 per cent has been obtained in a group of 76 patients who applied for treatment.—*Mary Frances Vastine, M.D.*

SAUER, HANS R., WATSON, ERNEST M., and BURKE, EUGENE M. Tumors of the testicle. *Surg., Gynec. & Obst.*, May, 1948, *86*, 591–603.

A review of 202 testicular tumors observed during a twenty-five year period is presented. In adopting the simplified classification of the Army Institute of Pathology (Friedman and Moore), the tumors were grouped as follows: seminoma (94), embryonal carcinoma (70), choriocarcinoma (3), teratocarcinoma (27), adult teratoma (5), and miscellaneous cell type tumors (3).

1. Metastases occurred in 117, or 57.9 per cent, of the cases. Their incidence was highest in patients with embryonal carcinoma (72.9 per cent) and lowest in those with seminoma (50 per cent). While metastases from seminomas remained quite often confined to the abdominoaortic nodes, it was the rule that embryonal carcinomas and teratocarcinomas metastasized also to the parenchymal organs.

2. Orchidectomy with regional lymph node dissection, followed by deep roentgen therapy, is advocated in the treatment of radioresistant testicular tumors and simple orchidectomy plus irradiation is preferred in the group of the more radiosensitive seminomas.

3. Indications, technique, and dosage of radiation therapy of testicular tumors are discussed. If metastases are present, favorable end results are obtained almost entirely in patients with seminoma or those with embryonal carcinoma plus seminoma. In contrast, response to roentgen irradiation is generally poor in patients with metastases from the other types of testicular neoplasms.

4. The end results obtained are presented: ninety-six (47.5 per cent) are alive and well,

2 are alive with disease, 95 died of the disease, 3 died of other causes and 6 were lost trace of. The five year cure rate was 48.9 per cent and the ten year cure rate was 34.7 per cent.

5. The following pattern of prognosis is presented. The prognosis is best in patients with adult teratoma or seminoma, particularly those that contain lymphoid stroma. It is less favorable in patients with teratocarcinoma or patients with embryonal carcinoma plus seminoma. The outlook is much more unfavorable in patients with tumors consisting of embryonal carcinoma with or without admixture of choriocarcinoma, and even worse in patients with plain choriocarcinoma.

6. In spite of certain shortcomings, the classification of Friedman and Moore is advocated as feasible because of its simplicity and because it is thought to promote a more common understanding among various investigators. However, in view of the difference in prognosis, it is suggested to divide embryonal carcinomas into tumors consisting of embryonal carcinoma plus seminoma and those of embryonal carcinoma in combination with other malignant cell structures.—*Mary Frances Vastine, M.D.*

BERMAN, LAWRENCE, and AXELROD, ARNOLD. Effect of urethane on malignant diseases; clinical, hematologic and histologic observations on patients with carcinoma, leukemia and related diseases. *Am. J. Clin. Path.*, Feb., 1948, *18*, 104–129.

Urethane therapy in 90 patients with various neoplastic diseases is reported. Favorable palliations in cases of carcinomatosis, lymphoblastoma and leukemia are noted. Urethane is most promising in androgen resistant carcinoma of the prostate and in chronic leukemia. Chronic myelogenous leukemia gives better results than chronic lymphatic leukemia. Decrease in size of enlarged lymph nodes, spleen and liver and reversion toward a more normal peripheral blood picture in leukemia was noted.

Nausea and vomiting in orally treated patients may be obviated by parenteral administration. Toxic effects include: hypoplastic anemia, leukopenia and thrombocytopenia. Possibility of hepatocellular damage needs further evaluation.

Undifferentiated leukocytes are affected more than differentiated forms. Erythroblastic tissue is more resistant than are either leukocytes or erythroblasts.

Hematologic improvement is not always accompanied by clinical improvement in chronic leukemia. Weight loss which is out of proportion to reduced caloric intake may represent important constitutional injury by urethane.

Repeated blood and bone marrow studies plus biopsy of tumors, lymph nodes, liver and spleen may aid in determining effects of treatment and mode of action of urethane.

Further investigation of urethane is warranted.—*Herbert Lobsenz, M.D.*

HERRMANN, JULIAN B., ADAIR, FRANK E., and WOODARD, HELEN Q. Effect of estrogenic hormone on advanced carcinoma of the female breast. *Arch. Surg.*, Jan., 1947, *54*, 1–9.

The authors report their experiences in treating 17 women with advanced carcinoma of the breast with estrogenic hormone. Ethinyl estradiol in doses varying from 0.15 to 0.7 mg. daily were used. Favorable responses were noted in approximately 40 per cent of the series. The favorable responses occurred predominantly in women over sixty years of age, whereas in younger women the estrogenic hormone seemed to accelerate the progress of the disease.

The patients who responded favorably showed evidence of improvement within the first four to six weeks of treatment. According to the authors, if no response was evident when this time had elapsed, there was little use in continuing the hormone.

Mild toxic reactions manifested by abdominal cramps and nausea were experienced by some early in the course of their hormone therapy. Vaginal smears studied in some patients revealed well developed estrus reaction. There were no changes in the serum calcium protein or alkaline phosphatase levels noted that could be ascribed to the daily administration of the ethinyl estradiol. A fall in the serum phosphorus level was observed in many patients, however.

The authors report in detail their experience in a patient forty years of age who was menstruating regularly to whom they gave the estrogenic hormone. The disease spread rapidly and suggested that it might have been the result of the specific action of the estrogen.—*Philip J. Hodes, M.D.*

MISCELLANEOUS

MARTIN, J. H. Radiation doses received by the skin of a patient during routine diagnostic

x-ray examinations. *Brit. J. Radiol.*, July, 1947, *20*, 279–283.

The skin dosage for various technical factors has been measured. A 70 kilovolt tube was used. At 20 milliamperes with the inherent filter and at 16 inch distance, the output is 175 roentgens per minute; at 30 inches it is 50 roentgens per minute. Adding 0.5 mm. of aluminum as a filter decreases the dose on the surface of a phantom 40 per cent with a concomitant drop of only 20 per cent on the surface of the film. With 1 mm. of aluminum added the skin surface dose drops 55 per cent while the film dose is reduced 30 per cent.

Data were collected from previous publications and from various hospitals in England as to the actual surface doses administered.

Chest: The long focal distance produces a low surface dose varying between 0.04 and 0.4 roentgen per exposure. The mean is 0.2 roentgen.

Intravenous pyelography: Doses range between 0.5 and 1.5 roentgen per exposure.

Skulls, sinuses: Four roentgens per exposure for the anteroposterior films and 1 to 2 roentgens for the laterals.

Gastrointestinal examinations: From 1 to 8 roentgens per film, with an average of 5 roentgens per film.

Spine: Ranges between 2 to 34 roentgens per film were found, with the average 5 roentgens.

Dental films: Because of the short distance the values vary from 1 to 15 roentgens per exposure with an average of 5. With the large number of films made there is usually overlapping, making this important.

Fluoroscopy: The average is between 50 and 100 roentgens for each five minute examination.—*E. F. Lang, M.D.*

Mitchell, J. S. Experiments on the mechanism of the biological action of fast neutrons using the summation method for lethal effects in mice. *Brit. J. Radiol.*, Sept., 1947, *20*, 368–380.

It has been previously demonstrated that although in general the biological effects of fast neutrons and gamma rays are similar, there are certain definite differences. In an attempt to determine whether the two types of radiation are completely additive and to determine the relative biological efficiency of the two, a series of experiments on mice was carried out. Lethal doses were used and various mixtures of gamma and fast neutron exposures were compared with doses which were similar in quantity but entirely of one type or the other. The particulars of the experiment are described in detail. Whole body irradiation was given.

The mixed doses are less effective than comparable doses of either fast neutrons or gamma radiation alone. This indicates a difference in the mechanism of action of these two radiations. An explanation is suggested. Since the relative efficiency of the two types of radiation varies with the duration of the treatment, it is thought that gamma rays act mainly on cells in the prophase of mitosis, and are thus relatively more effective if the treatment is prolonged. Fast neutrons, affecting the cells not only during mitosis but even during the resting stage, do not need a long exposure for significant effect.

A section is included on dosimetry of fast neutrons.—*E. F. Lang, M.D.*

Lewis, Margaret Reed. In vivo staining and retardation of tumors in mice by acridine compounds. *Am. J. M. Sc.*, March, 1948, *215*, *282*–289.

Three hundred and thirty-one acridine compounds were administered orally to tumor-bearing mice in known per cent of dry weight of their food. Two hundred and four stained tumor tissue and the majority of those that colored tumors also somewhat retarded their growth. The administration of acridine compounds did not prevent tumor growth or bring about regression of growing tumors. It simply slowed the rate of multiplication of tumor cells.

The majority of the 9 amino acridines that stain tumor tissue as well as retard its growth show dialkyl-amino-alkyl-amino chains in the nine positions.—*Herbert Lobsenz, M.D.*

Lasnitzki, Ilse. A quantitative analysis of the direct and indirect action of x radiation on malignant cells. *Brit. J. Radiol.*, June, 1947, *20*, 240–247.

Mouse adenocarcinoma 63 is a transplantable small cell carcinoma. A number of mice were inoculated with this tumor and the growths were examined microscopically at various intervals after irradiation. Tissue cultures of the same tumors were irradiated with similar doses and examined at similar intervals.

The effects common to both tumors and cultures were previously reported and are: absent and irregular mitosis, increase in cell size, and the appearance of degenerative cells. Vascular

reaction of a severe nature was demonstrated in the tumors with the sublethal dose which was used.

An analysis of the present data revealed that changes occurring during the first day are the result of direct action on the malignant cells. These changes are the appearance of degenerative cells and absence of mitosis. After the second day the number of mitoses in the tumor rapidly builds up but there is much slower return of mitosis in the culture. The actual level of mitosis in the tumor is low, however, and no further increase occurs; in the culture return of mitosis is quite slow but it returns to a normal level. Many more degenerative cells appear in the six days after the first in the tumor but not in the culture. Mitosis in the tumor is only 39 per cent of that in the culture, while degeneration in the culture is only 35 per cent of that in the tumor.

Thus, although in the two types of malignant cells the results of irradiation are qualitatively similar, they vary in quantity and in time of appearance. In the tumor early mitotic recovery and development of degenerative cells is dependent upon the intact blood supply, but after the second day the irradiation-induced vascular damage produces failure of total mitotic recovery and increase in degenerative cells. About one-third of the total effect is due to the direct action and two-thirds to the indirect action of the irradiation.—*E. F. Lang, M.D.*

WOLFF, BRIGITTE, and ELLIS, FRANK. Quantitative histological analysis of radiation effects in human carcinomata. *Brit. J. Radiol.*, Sept., 1947, *20*, 381–386.

Biopsies of tumors made before, during and after roentgen treatment can be used to determine the response to irradiation. Cells are counted in selected areas and classified into four categories: resting, dividing, differentiating and degenerative cells. The change in the ratio of the cells in these groups indicates the response of the tumor to treatment.

A series of 37 tumors was examined by biopsies taken immediately before treatment and then after seven, fourteen, and, in most cases, twenty-one days. The response as determined from the biopsies was compared with the response as estimated clinically. It was found that in some cases of poor histological response with good initial clinical response, later observation showed that the clinical course was retrogressive after some interval. In other words, the longer the period of observation, the more agreement there was between the clinical and histological findings.

In this series of 37 cases there was agreement in 92 per cent of those observed for fifteen months or more. In the 6 cases where there is disagreement, each tumor was at a site where slow-growing cancers usually arise.

This method of examination is suggested not only as a means of establishing prognosis after roentgen therapy, but also as a method of determining rapidly which treated tumors will not respond so that they may be attacked surgically before too late.—*E. F. Lang, M.D.*

HOWARTH, FRANK. Isotopes and radiation hazards. *Lancet*, July 10, 1948, *2*, 51–53.

This paper is intended as a warning to those British physicians who are now beginning to have radioactive isotopes available for experimental use. It contains a fairly good review of the literature on this subject.—*J. S. Summers, M.D.*

MOORE, FRANCIS D. The use of isotopes in surgical research. *Surg., Gynec. & Obst.*, Feb., 1948, *86*, 129–147.

Although the types of biological research which may be carried out with radioactive isotopes are many, they tend to arrange themselves into several significant subheadings.

1. *Permeability and Membrane Transfer.* In the study of the penetration of ions or molecules from one area of the body fluids to another, isotopes make their greatest fundamental contribution to research. Whether the interposing membrane be the capillary, the lymphatic, the cell, the nucleus or some special barrier such as the glomerulus or choroid plexus, and whether the tracer be an ion or a large protein molecule, isotopic techniques inform the investigator of the relationships between the two sides of the membrane in a fashion which cannot be gained in any other way.

2. *Tracing Metabolic Pathways.* Though we can dissect a whole animal and analyze its constituent organs chemically for an element, we have no way of knowing the previous position of the element as found in the various organs, nor its distance in point of time or metabolic pathway from its source, such as the gastrointestinal tract. By the use of a tagged element it is possible to give one radioactive dose to the organism and at varying periods after administration to analyze the animal and find

the position in the various organs and body fluids of this single dose. When one has analyzed the whole organism some hours after a feeding containing a radioactive element, the distribution which one finds is presumably typical for the distribution of any similar amount of stable element administered the organism.

3. *Utilization by Specific Organs.* As a refinement of the above investigation, it is possible by means of isotopes to study the utilization of elements or compounds by specific organs. An outstanding example of this is the utilization by the thyroid of iodine.

The autoradiograph presents the most intimate picture of utilization of elements or compounds by specific tissues, and belongs in this category of observation. The autoradiograph is a record made on photographic emulsion by the beta radiation of isotopes previously administered to the animal or patient; by comparison with microscopic slides and suitable magnification, exact histochemical localization of isotopes may be obtained.

4. *External Localization.* The concept of injecting a radioactive substance into an animal or a patient, and then casting about over the living organism with a Geiger counter to find out where the element went, has gripped the imagination of investigators for many years. In the case of the thyroid the selective localization of the radioiodine in thyroid tissue, whereever that tissue is, has provided again, by coincidence, a ready application of such methods. Studies of the circulation by externally placed counters, using Na, have also been carried out. Here, however, the lack of selective localization makes interpretation much more difficult.

5. *"Tagging" of Complex Compounds.* Attempts to label complex organic compounds with radioactive isotopes go back to the earliest days of the cyclotron. Many important molecules which contain such elements as carbon, phosphorus, iodine, iron, or sulfur and which were susceptible of synthesis, could by synthethesized with the radioelement in place of its stable isotope.

6. *Fluid Space Measurement.* The measurement of volumes of body fluid available for the solution of an ion may be carried out by dissolving a tracer for that ion in the body fluid space in question, allowing mixing to occur, making appropriate corrections for excretion and then studying the final dilution obtained.

7. *Therapy with Radioactive Isotopes.* This is an application of radioactive isotopes dependent upon selective localization in pathologic tissues.—*Mary Frances Vastine, M.D.*

Elkin, Daniel C., Cooper, F. W., Rorher, R. H., Miller, W. B., Shea, Patrick, and Dennis, E. W. The study of peripheral vascular disease with radioactive isotopes. Part I. *Surg., Gynec.& Obst.*, July, 1948, *87*, 1–8.

Radioactive sodium carbonate is received from the pile at Oak Ridge, Tennessee. The mass obtained weighs 0.3 gram and is rated 35–110 milliroentgens of gamma radiation per hour at 24 inches from source of gamma radiation. This material is converted into sodium chloride by the addition of hydrochloric acid. Neutralization is effected by titration with sodium hydroxide. The resulting sodium chloride solution is evaporated to dryness and is redissolved in pyrogen-free distilled water, and sterilized by autoclave. Dilutions of the material are made depending upon the proposed method of utilization.

Two methods of study were employed.

1. The first method described by Smith and Quimby involves the "build-up" of radioactive sodium in the tissues of the extremities following its intravenous injection in the arm.

2. The other method was suggested by Kety. It is a relative flow determination based on the rate of disappearance of radioactive sodium when injected intramuscularly.

The latter method has been utilized in 115 individuals both normal and with vascular disease. It has been used in normal individuals to evaluate the effect of certain drugs and other measures reputedly effective in enhancing the circulation in the extremities. Similarly it has been used in the evaluation of patients with vascular disease and their response to therapy. These observations are to be reported at a later date.—*Mary Frances Vastine, M.D.*

Sievert, Rolf M. The tolerance dose and the prevention of injuries caused by ionizing radiations. Silvanus Thompson Memorial Lecture. *Brit. J. Radiol.*, August, 1947, *20*, 306–318.

The important physiological effects of ionizing radiations are in the skin, the blood and blood forming organs, and the gonads and germ cells. A minimal erythema is produced by 200 to 600 roentgens given in one dose, and an exposure ten times as great produces skin necrosis. Protraction and fractionation both decrease the effect on the skin.

Determination of the extent of injury to the blood cells is more difficult to assess. A preliminary study has shown that hypersegmentation, pathological lymphocytes, granulocytopenia, and a shift to the left are the most marked changes to be demonstrated in the peripheral blood. Effect on the gonads is also difficult to determine. Sterility occurs long after blood changes develop. Genetic changes can be determined only with long, exact statistical studies.

The term tolerance dose may be used to describe either that dose which produces barely perceptible biologic effect (active tolerance dose) or the maximum allowable dose for radiological workers (safety tolerance dose). The active tolerance dose cannot be determined at present because of the variation in standards, the difficulty in obtaining standard conditions, and the necessity of experimentation on man. As the safety tolerance dose should be determined on the basis of this, its determination also is at present a matter of opinion. The limits of the tolerance dose may be based on the effect on the skin, when the longer wavelengths are considered, or on the effect on the body as a whole with the shorter wavelengths, in which case the action on the blood is used.

The skin tolerance dose may be estimated by adjustment of the figure arrived at by extrapolation of a fractionation curve to a very small daily dose. The safety tolerance dose thus arrived at is between 0.1 and 0.5 roentgen per day. This is in agreement with figures obtained by other methods. Determination of the blood tolerance dose is more difficult. By grouping roentgen-ray workers into four groups, according to the risk involved in their daily work, and examining their blood, it was found that daily doses of from 0.02 to 0.05 roentgen can give rise to blood changes.

The effects of small doses on animals and plants have been determined, but these unfortunately are not directly applicable to man. Intensities as low as 0.001 to 0.005 roentgens which is in the range of the normal ionization existing in nature, have been shown to produce changes is growth rate and in timing of life cycle.

Irradiation can be measured for these tests photographically, with a fluorescent screen, with ionization chambers, or with Geiger-Müller counters. In many cases, however, particularly in diagnostic work, it is only when actual leaks in protection are discovered that the measurements are meaningful. With a negative reading, one cannot be certain that the involved personnel are acting normally, or that all the leaking radiation is being measured. The best control method is rigid inspection, control of working technique, and regular blood counts.

In Sweden, control of radiological work has been established by law and regular inspections are carried out. The most dangerous conditions are those in a small roentgen department without a radiologist where risk is neglected, in large establishments where protection is sacrificed for efficiency, and where much work is done on insane individuals or children. The risk of dental equipment, because of the unprotected primary beam, has been underestimated.—*E. F. Lang. M.D.*

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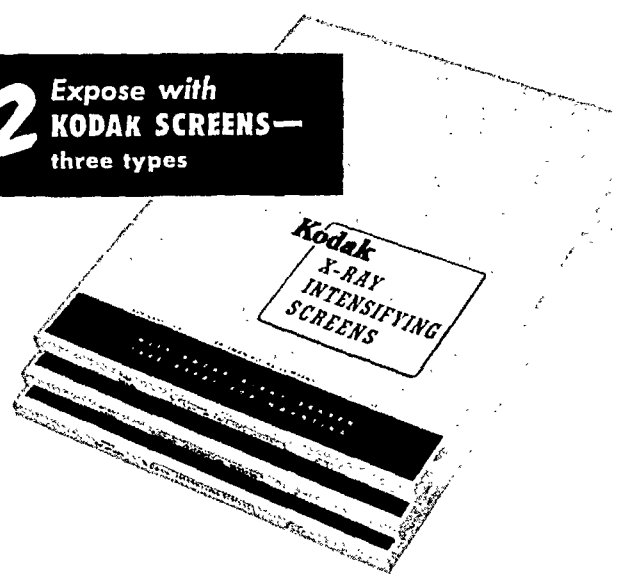


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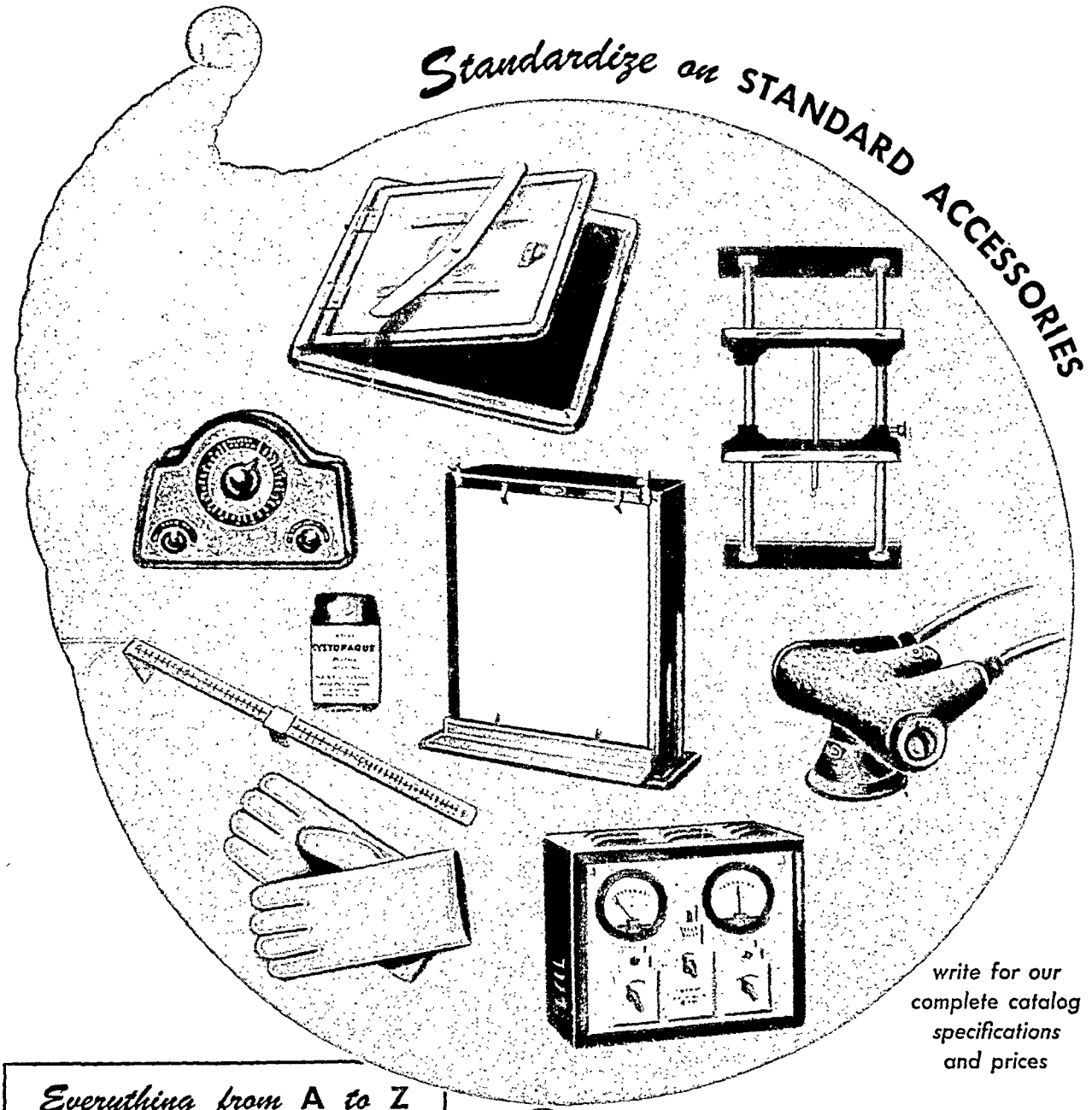
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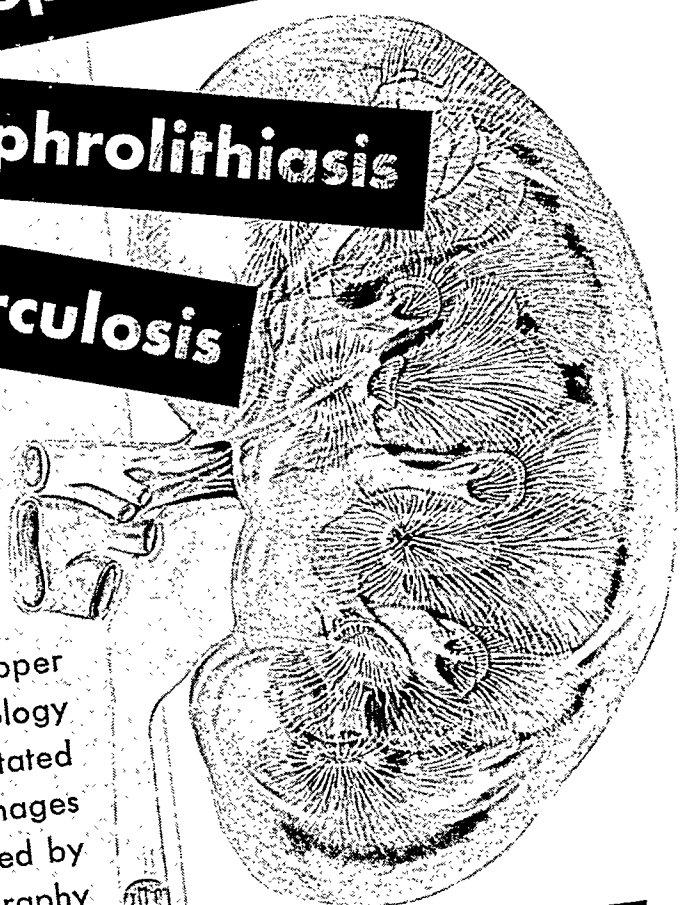
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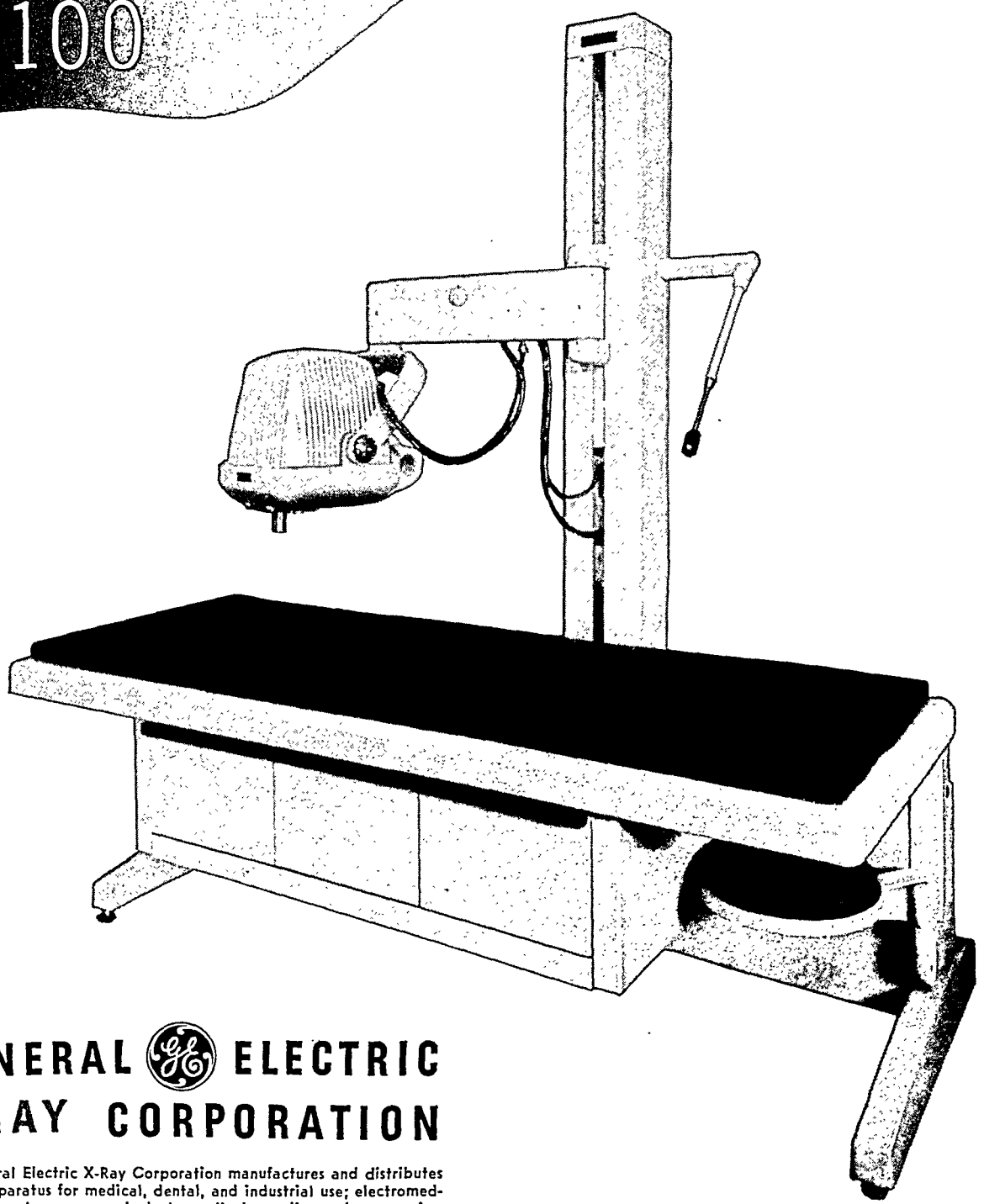
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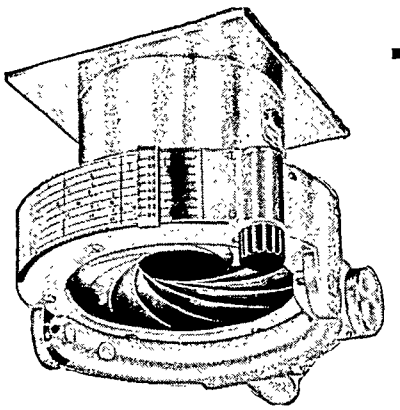
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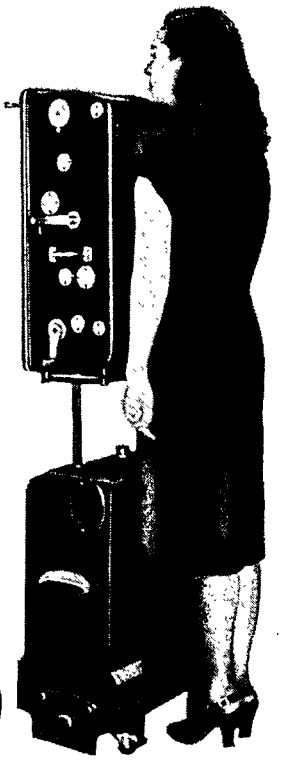
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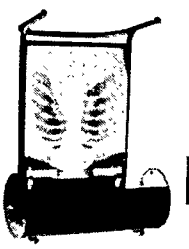
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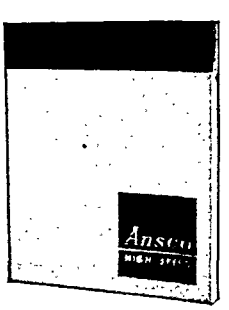
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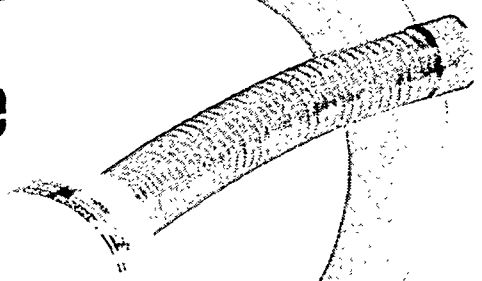
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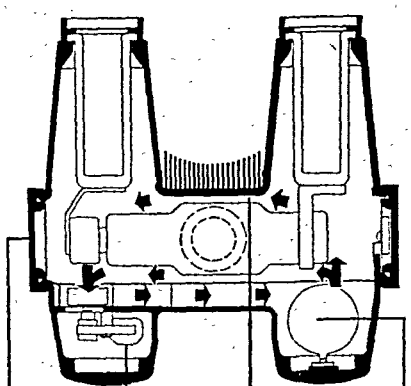
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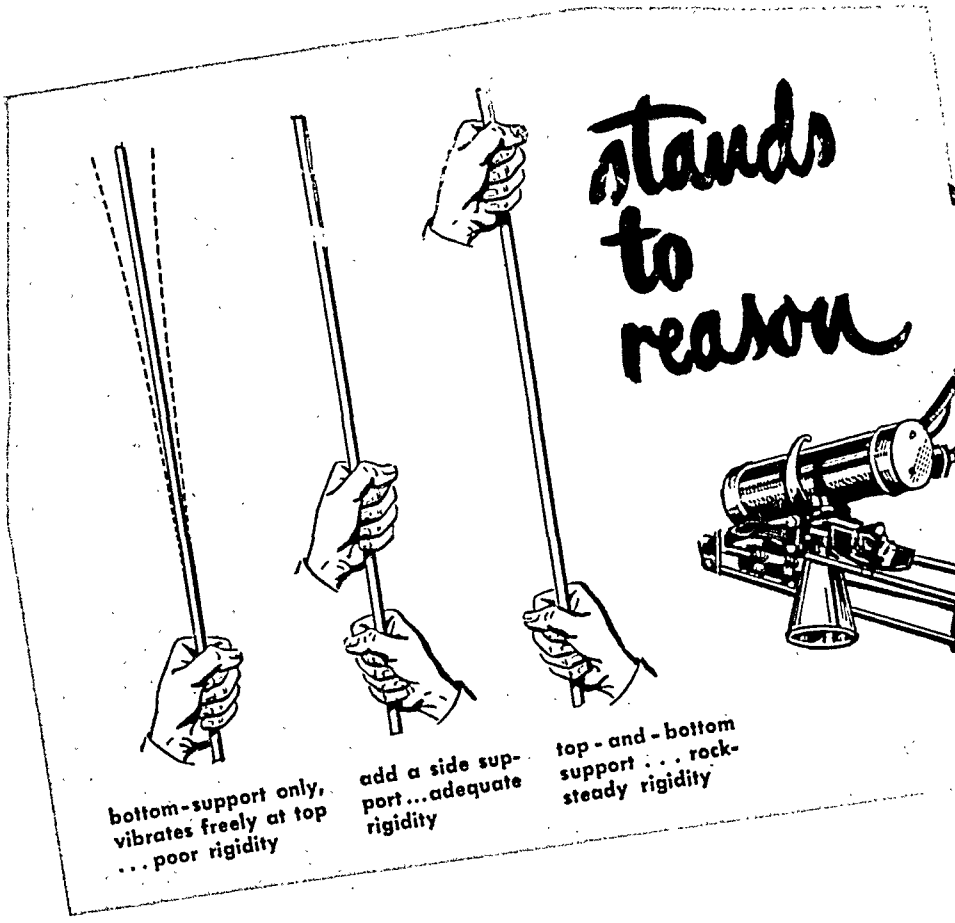
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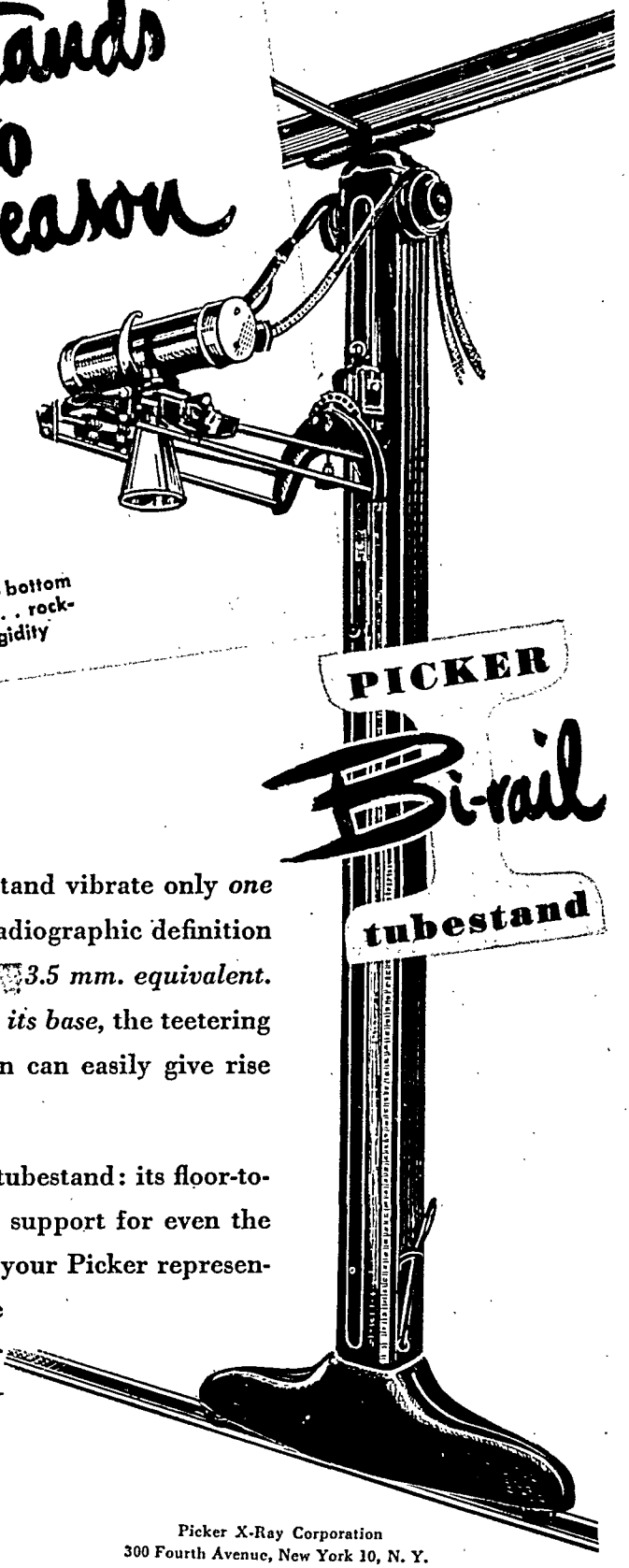
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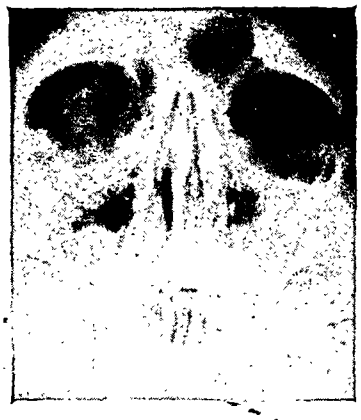
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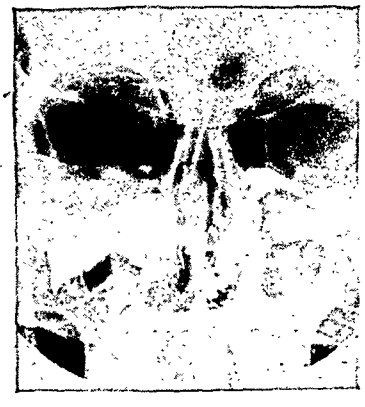
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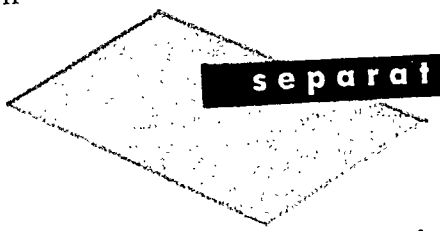
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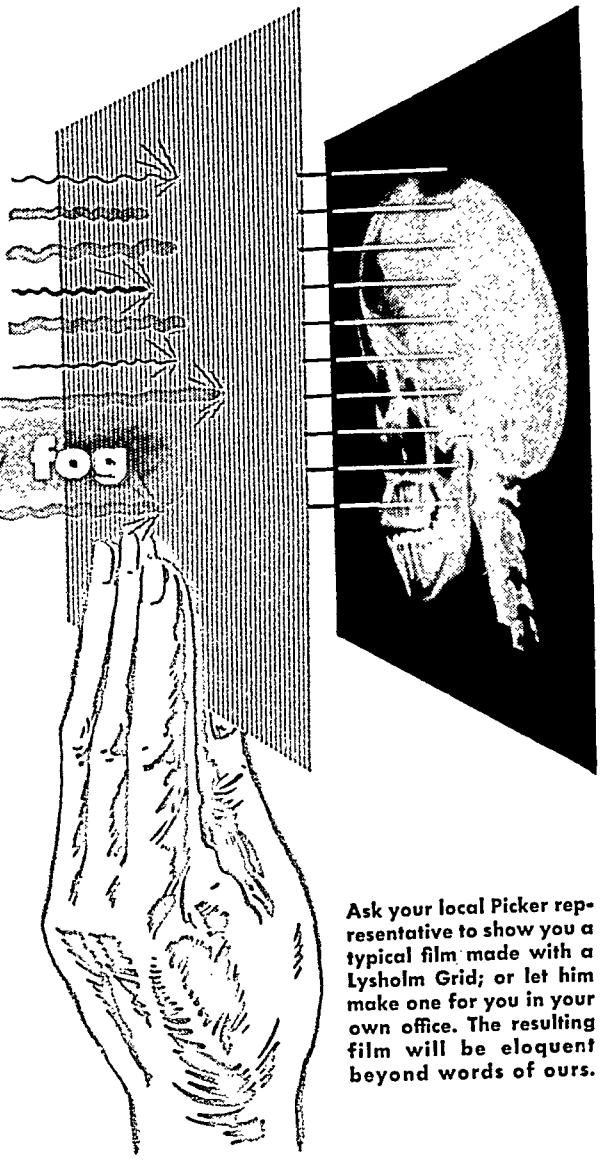
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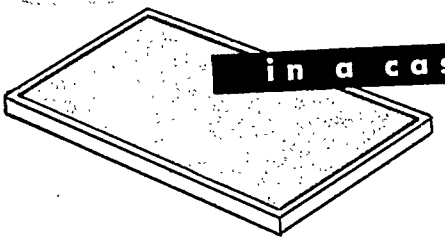
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CONTENTS

Hemosiderosis of the Lung Due to Mitral Disease EUGENE P. PENDERGRASS, M.D., EDWIN L. LAME, M.D. AND HERMAN W. OSTRUM, M.D. 443

The Apical Form of Bronchopulmonary Cancer DR. NICOLÁS ROMANO AND DR. RODOLFO EYHERABIDE 457

A Case of Carcinosarcoma of the Esophagus ARTHUR PURDY STOUT, M.D., GEORGE H. HUMPHREYS, II, M.D., AND LOUIS A. ROTTENBERG, M.D. 461

Mass Roentgenological Survey of the Gastrointestinal Tract to Detect Cancer of the Stomach SHERWOOD MOORE, M.D. 470

Paraplegic Neuroarthropathy JULIUS SOLOVAY, M.D., AND H. U. SOLOVAY, M.D. 475

Double Contour, Cupping and Spurring in Roentgenograms of Long Bones in Infants KURT GLASER, M.D. 482

Sesamoid Bones of the Hands and Feet . . . CHARLES A. HUBAY, M.D. 493

Occupational Calcareous Peritendinitis of the Feet CLARK F. MILLER, M.D. 506

Kaposi's Sarcoma WILLIAM H. BOONE, M.D., AND EMIL A. KRATZMAN, M.D. 511

Radium Therapy for Carcinoma of Bartholin's Glands HARRY H. BOWING, M.D., ROBERT E. FRICKE, M.D., AND THOMAS J. KENNEDY, M.D. 517

Effects of Repeated Low Doses of Neutrons on the Estrous Cycle of the White Rat JAMES L. LEITCH, PH.D., DOUGLAS M. GAY, M.D., AND GEORGE A. NEVILLE 530

Pharmacological Reactions of Sera and Drugs Irradiated with Roentgen Rays of Varying Wavelength . . . DAVID I. MACHT AND MARCUS OSTRO 534

Thimble Chamber Calibration on Soft Roentgen Rays . . . F. H. DAY 543

A Negative Feedback Dosage Rate Meter Using a Very Small Ionization Chamber . . H. E. JOHNS, E. K. DARBY, AND J. J. S. HAMILTON 550

Department of Technique

Roentgenographic Facsimile: A Rapid Accurate Method for Reproducing Roentgenograms at a Distance via Wire or Radio Transmission J. GERSHON-COHEN, M.D., AND A. G. COOLEY 557

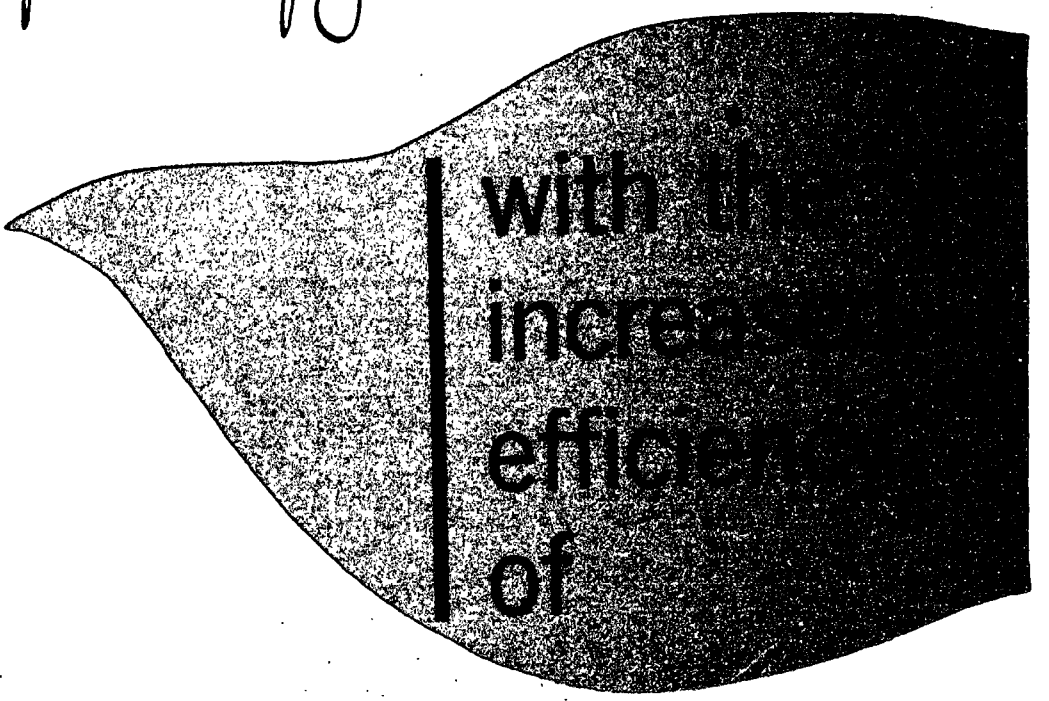
Editorial

Gastric Vascular Shunts 561

Society Proceedings, Correspondence and News Items 565

Abstracts of Roentgen and Radium Literature 572

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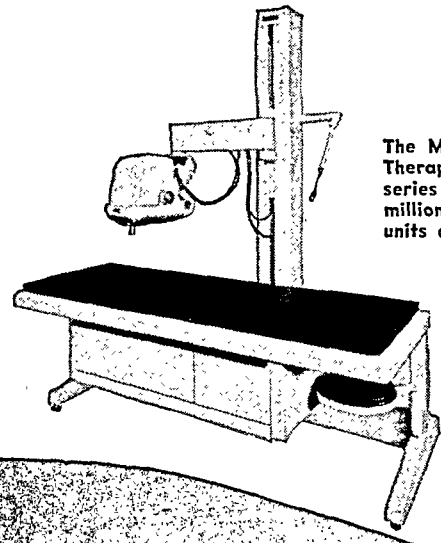
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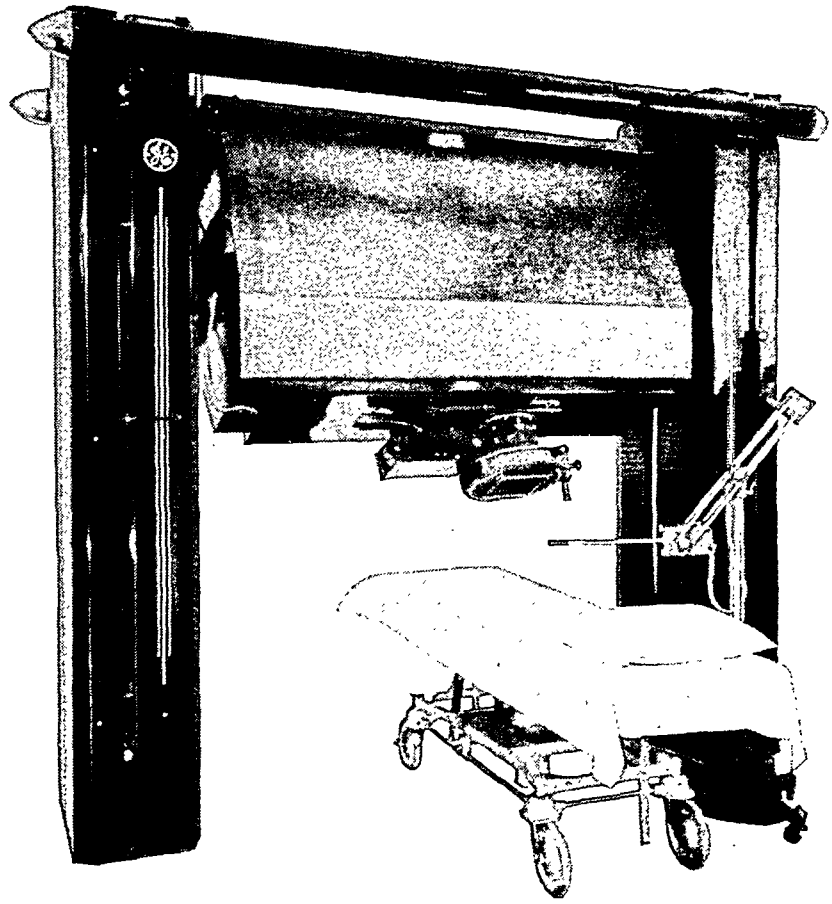
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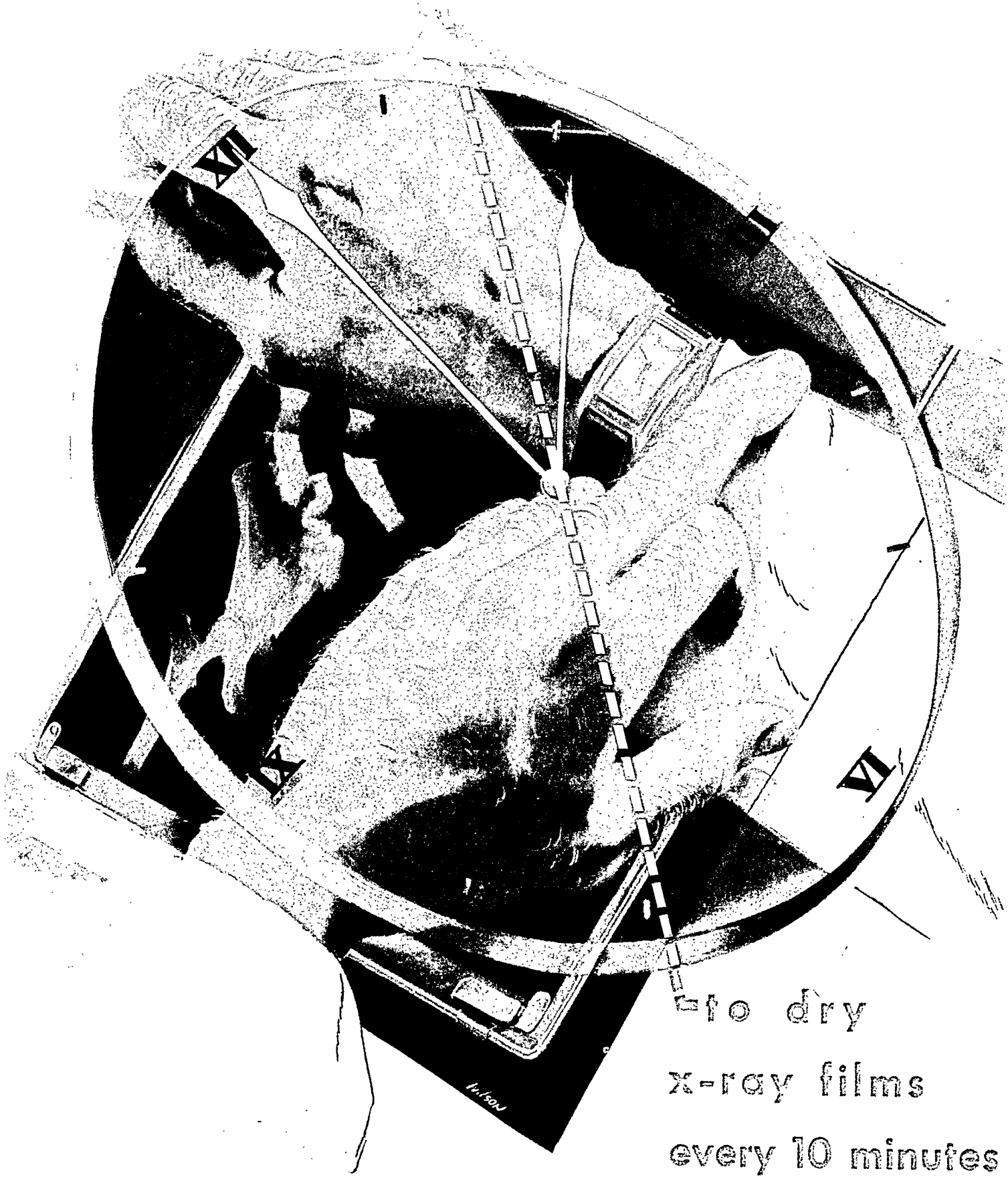
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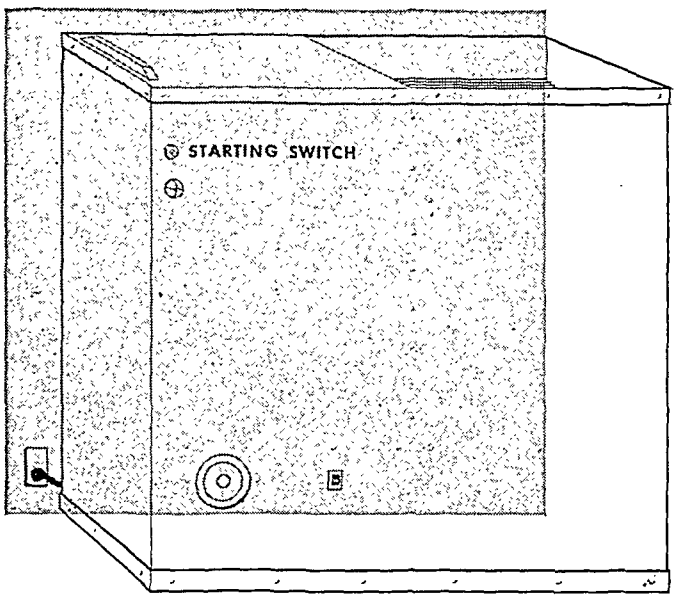
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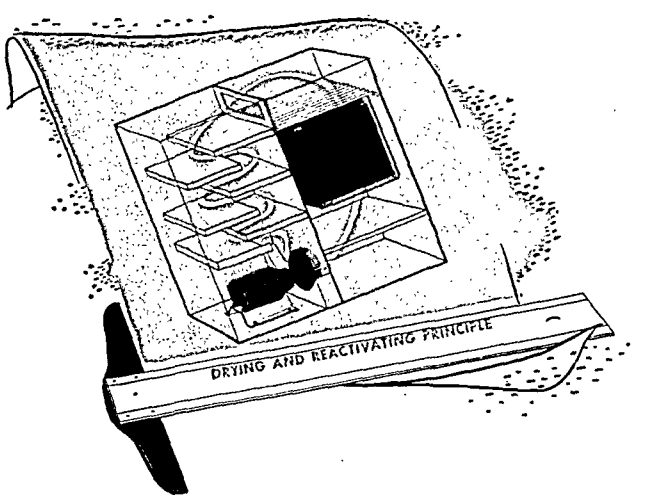
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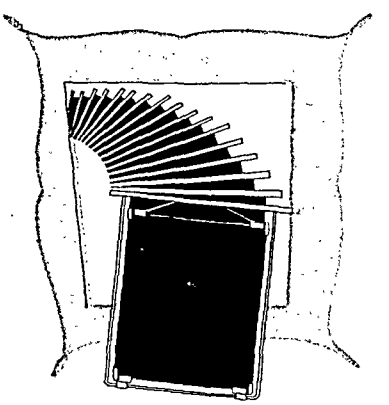
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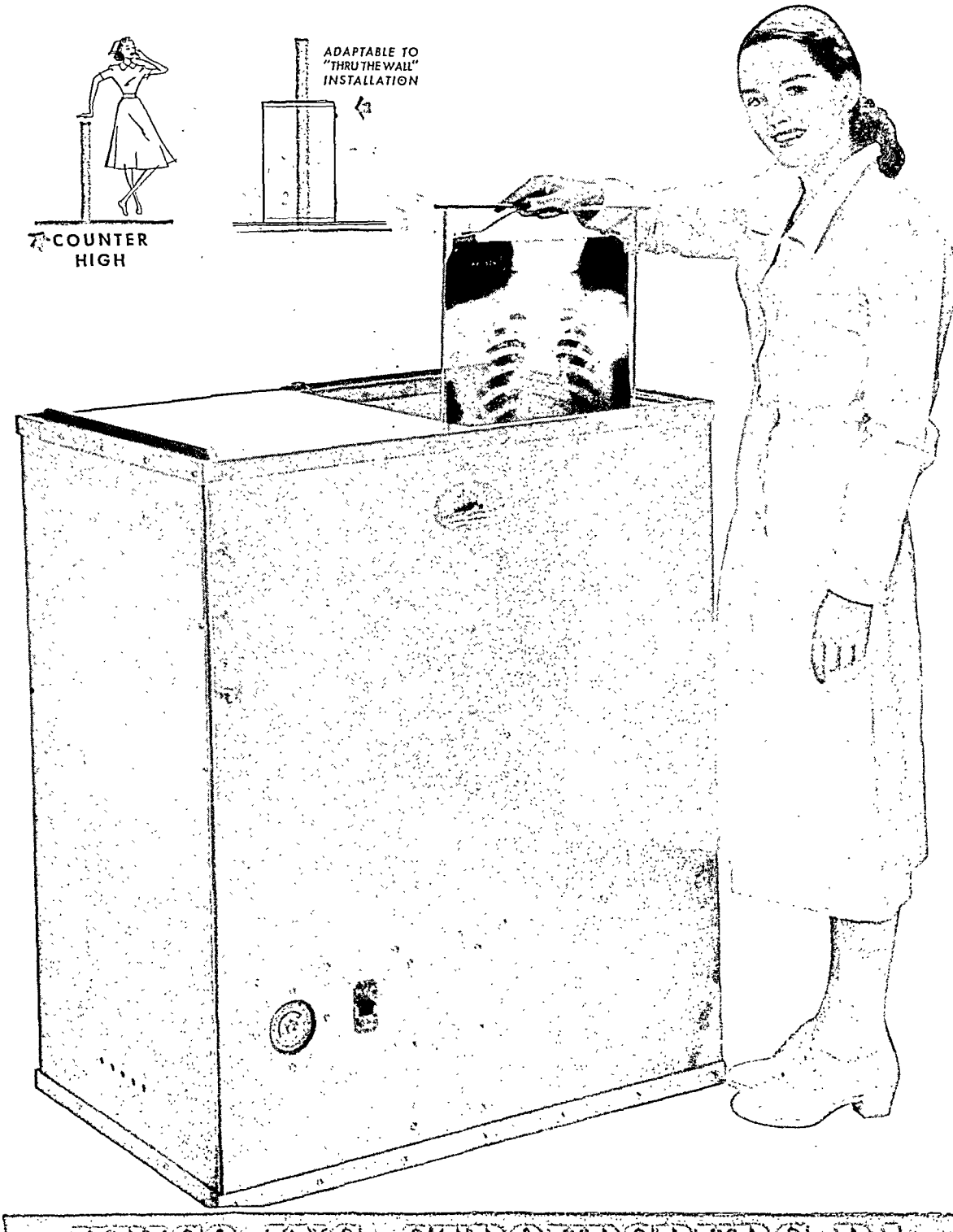
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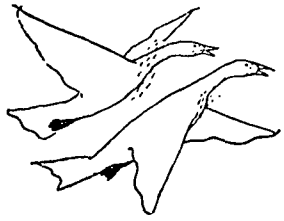
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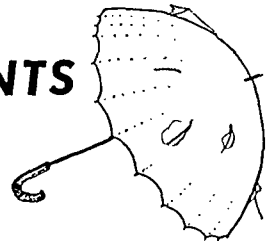
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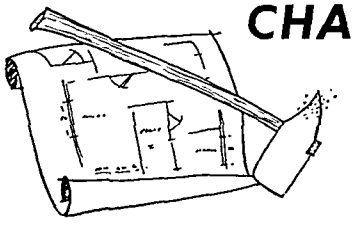


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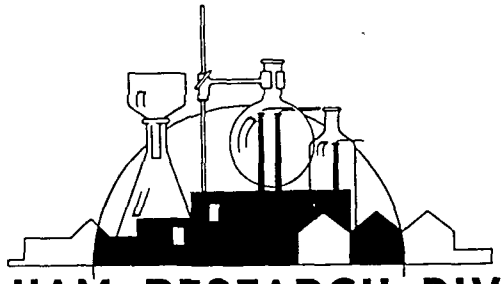




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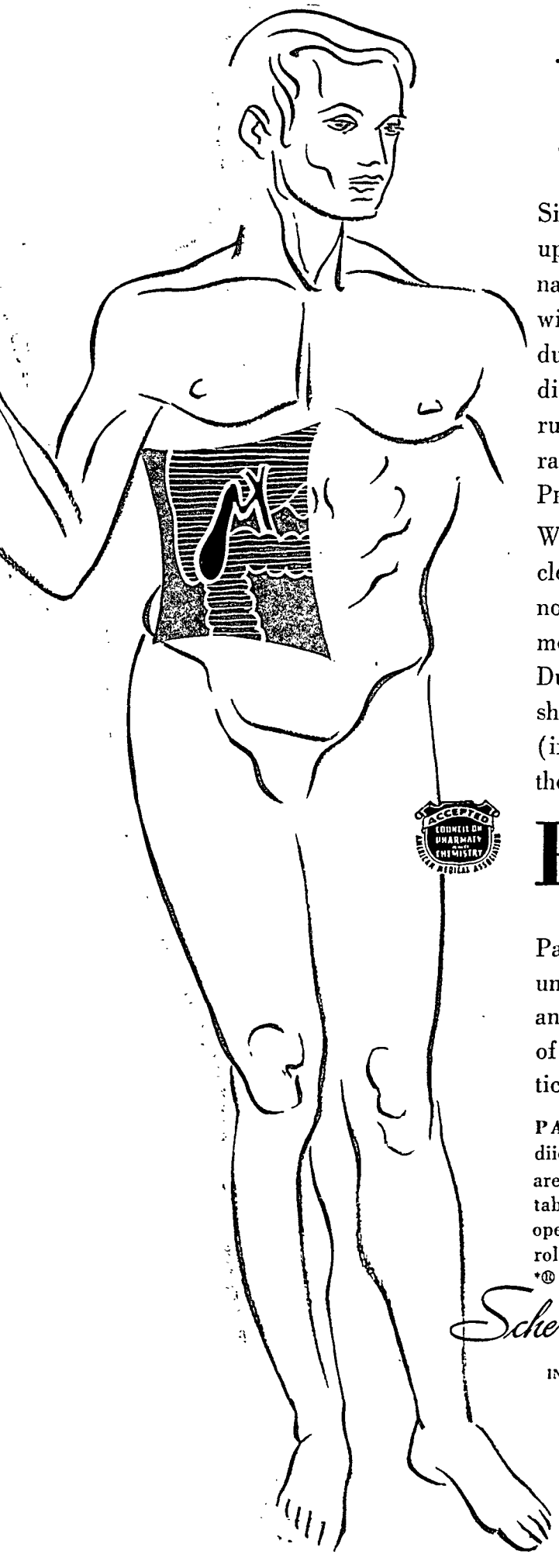


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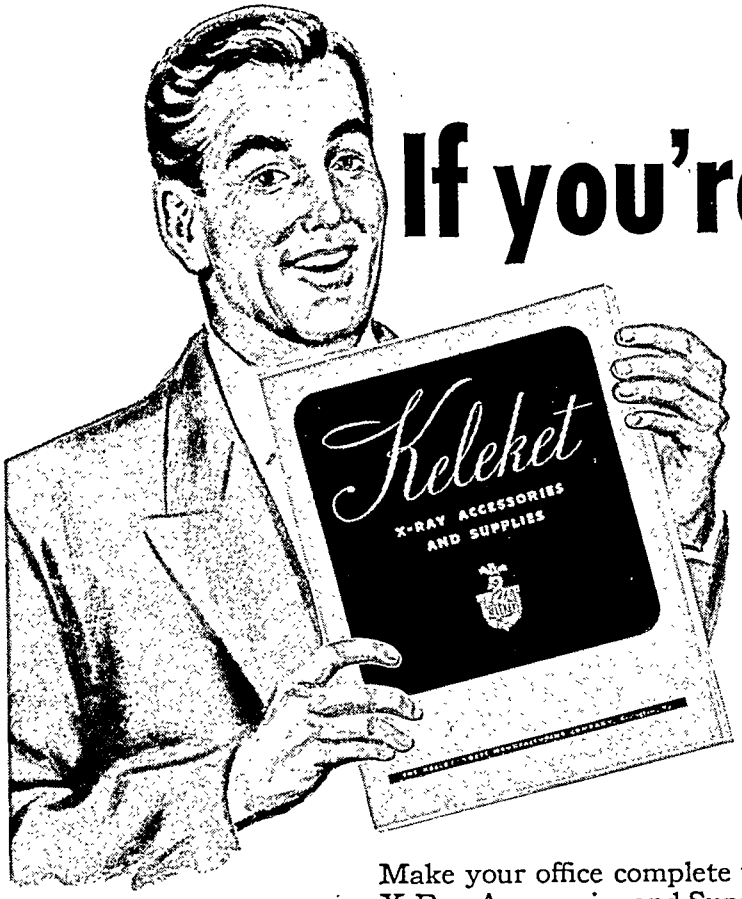
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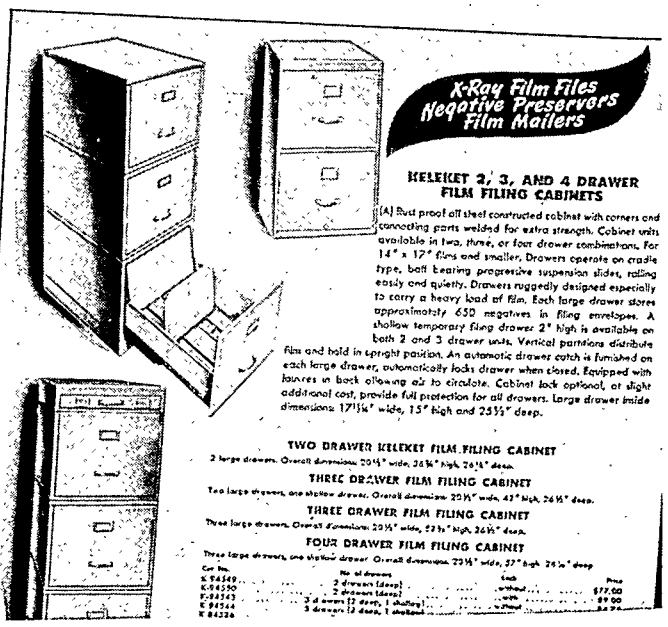
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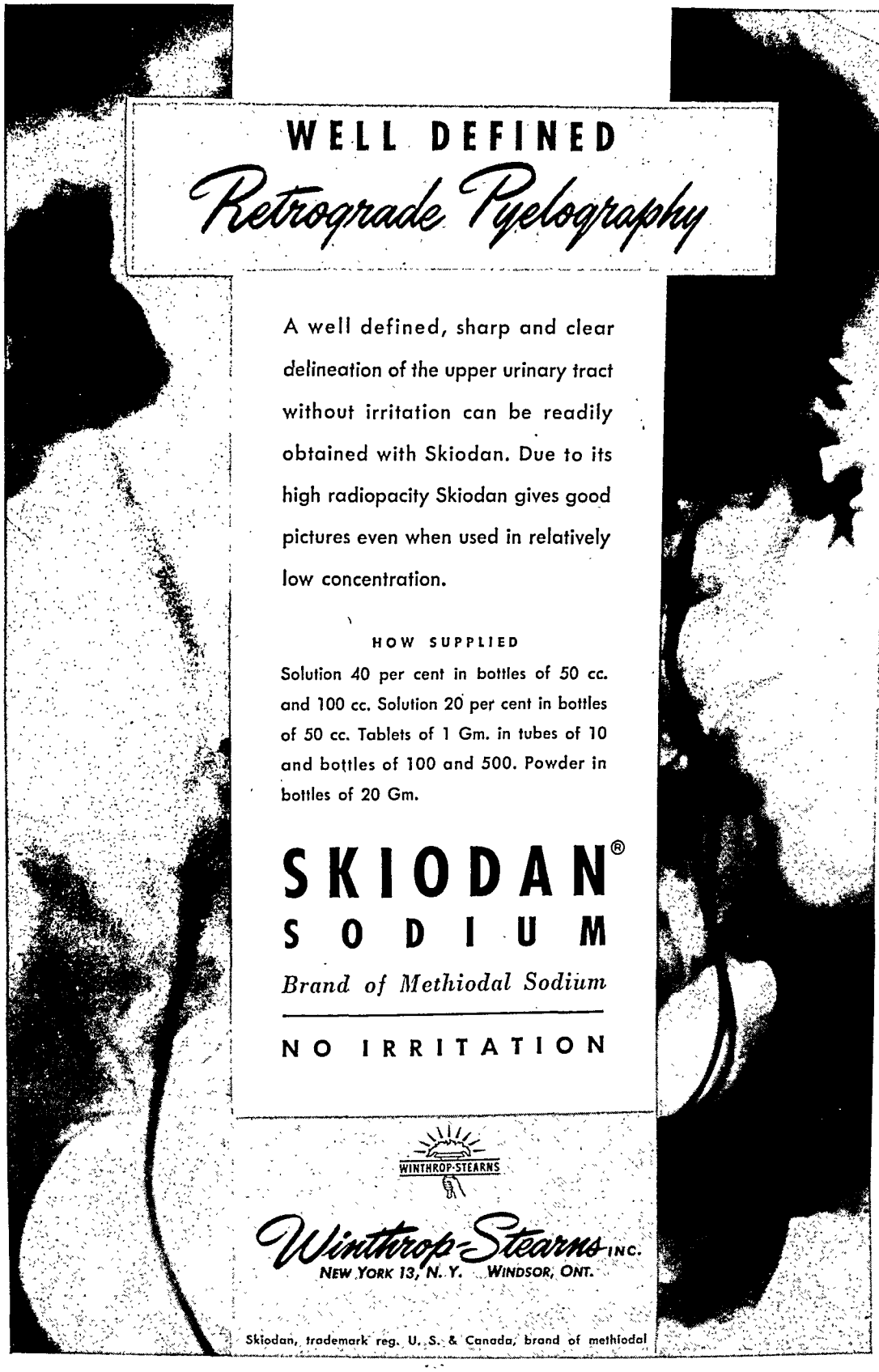
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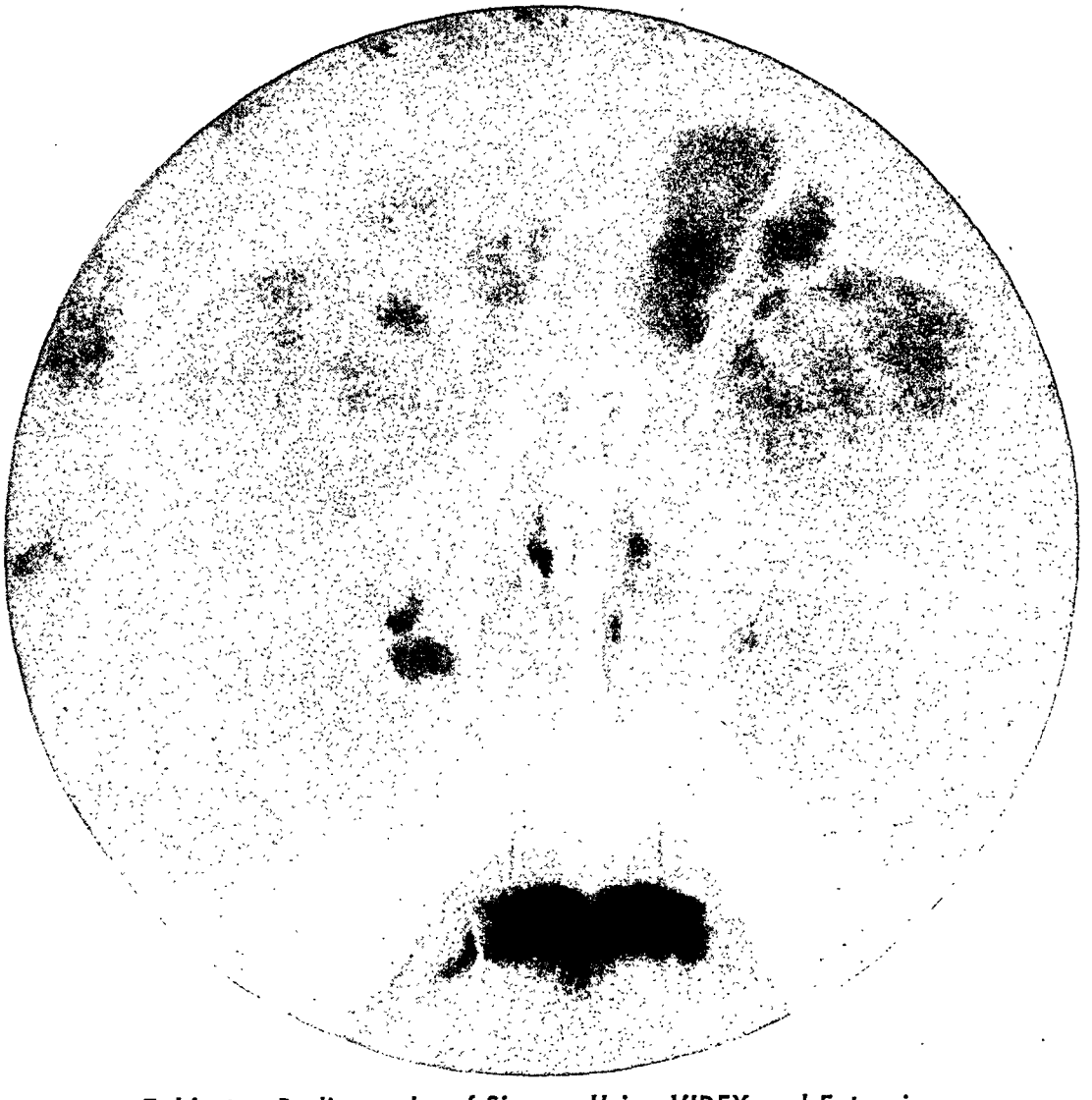


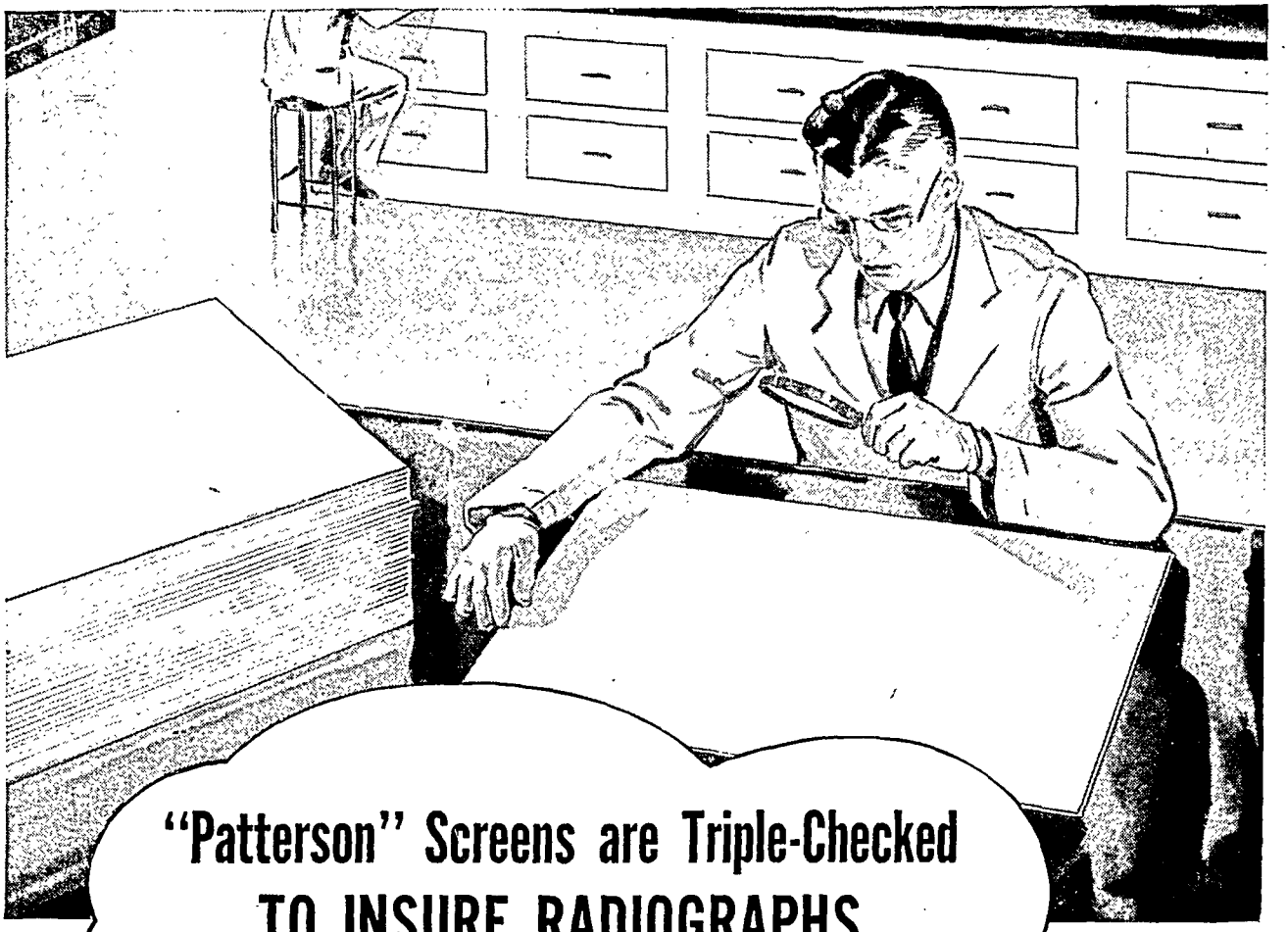
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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 61 APRIL, 1949 No. 4

HEMOSIDEROSIS OF THE LUNG DUE TO MITRAL DISEASE

A REPORT OF SIX CASES SIMULATING PNEUMOCONIOSIS*

By EUGENE P. PENDERGRASS,† M.D., EDWIN L. LAME,** M.D.
and
HERMAN W. OSTRUM,‡ M.D.
PHILADELPHIA, PENNSYLVANIA

THIS report deals with mitral valve disease accompanied by the deposition of hemosiderin in the lungs, in such a fashion that roentgenograms reveal a fine nodulation much like pneumoconiosis or miliary tuberculosis. We have a thirteen year and a four month roentgen observation on 2 living patients carrying this lesion; and have found 4 autopsied cases of similar nature which provide the histopathologic explanation.

Such cases are very rare. From the United States there is no autopsied case reported; and from the world literature a total of 17 autopsied cases previous to those disclosed herein. Not all of the 17 demonstrated a clear granular roentgen pattern. Rosenhagen, in 1928, probably is the first to have described the roentgenology together with the histopathology. Since then, Pedro Pons and Amell Sans, Anglin, Munk, Roche, Scott, Park and Lendrum, and others,[12,33,41] have added to the meager record. Pendergrass and Leopold predicted that one of our living cases would prove to be such a lesion. Sosman has discovered one case with autopsy, which he is allowing us to report at this time.

Nodular lung lesions seen in roentgenograms and confirmed histopathologically as siderosis have been described in several categories. Arc welders may inhale iron-laden fumes to such an extent that lung roentgenograms reveal a diffuse nodular pattern caused by the deposition of the metal.[7,9,18,35] Silver finishers, working in rouge (iron oxide), are subject to a similar lung deposit of an iron compound.[20] Grinders of ferrous metal, not exposed to silica, have been shown[27] to carry a fine granular lung lesion, which appears roentgenographically very much as nodular silicosis. These three groups are examples of exogenous siderosis of the lungs.

Endogenous pulmonary siderosis is exemplified by our group of mitral heart disease patients and by the children who suffer severe anemias[2,8,28,39,40] and die with hemo-

* From the Departments of Radiology, Hospital of the University of Pennsylvania,† the Presbyterian Hospital of Philadelphia,** and the Philadelphia General Hospital.‡ Presented at the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14–17, 1948.

siderin nodules in the lungs. These lesions, too, have been demonstrated in roentgenograms.

Brown induration of the lung, resulting from hyperemia and congestion, accompanied by calcification and bone formation, is more often found in mitral disease.[11,13,14,34,42] The small irregular densities seen in such roentgenograms are due to the calcium or bone and not to iron compound.

All of the foregoing patients demonstrate diffuse nodular densities in lung roentgenograms that suggest miliary tuberculosis or the more common pneumoconioses.

REPORT OF CASES

Case 1. J. S. (Fig. 1 and 2), male, white, aged thirty-three. Interest in this subject was aroused by the discovery of this man's roentgenograms by one of us (E. P. P.) at the Hospital of the University of Pennsylvania. In 1931, at the age of sixteen, he spit blood. Rheumatic endocarditis was found. He had

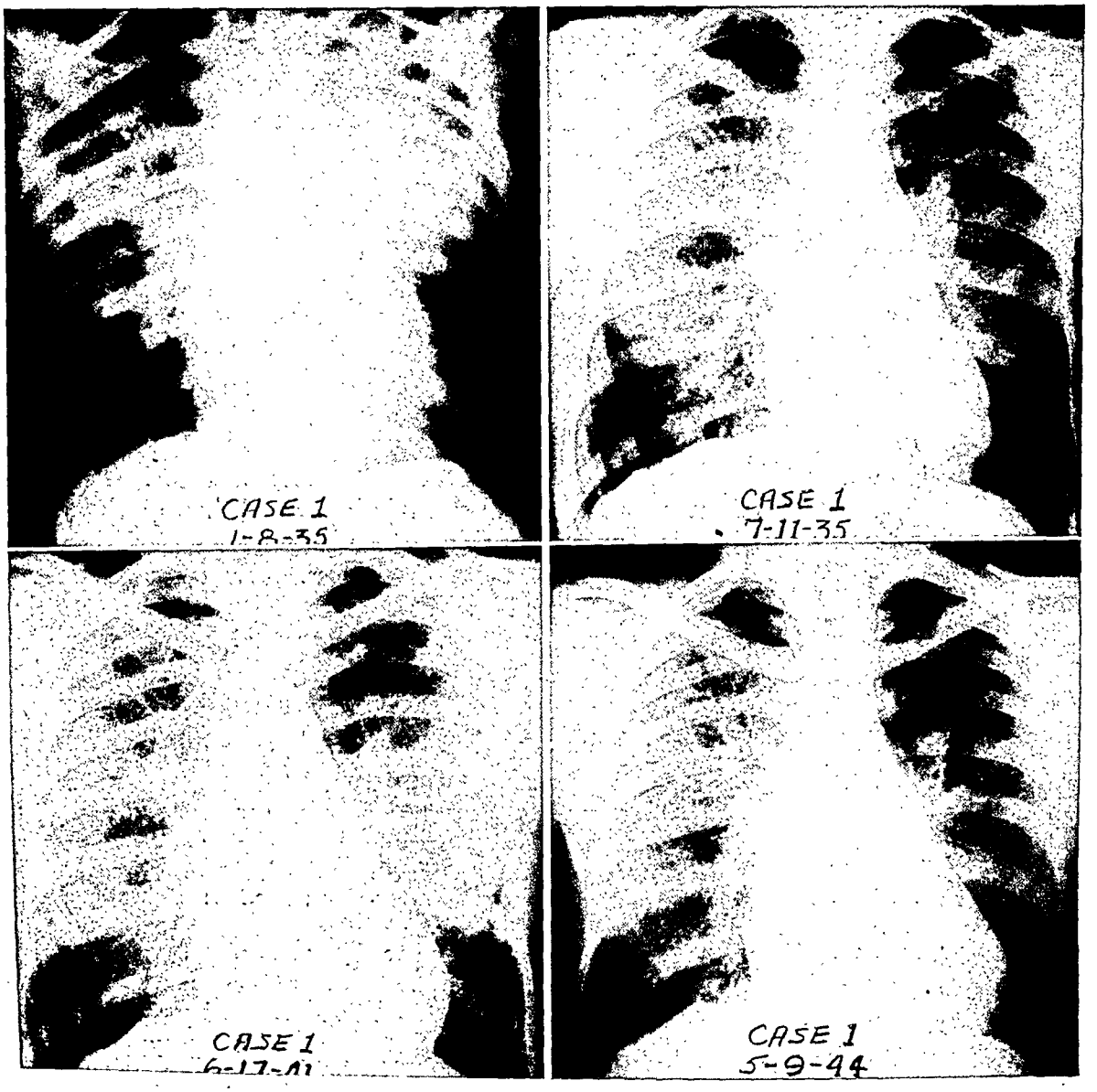


Fig. 1. Case 1. J. S. Representative roentgenograms from a thirteen year observation. Marked generalized nodulation present at first acquaintance when a pneumonia existed. Subsequent studies show an increased prominence of nodules and then a static condition, except for added cardiac enlargement.



Fig. 2. Case 1. J. S. Continuation of Figure 1. The magnified portion of lung demonstrates the irregular, non-circular character of the fine lesion.

other attacks from 1932 to 1934 and in late 1934 suffered a type IV pneumococcus pneumonia, when his chest roentgenograms demonstrated a bilateral pneumonic lesion. At that time, there was a generalized nodular lesion in addition, which we believe antedated the acute disease. Since then, all studies have revealed this fine nodular pattern resembling miliary tuberculosis or pneumoconiosis. In 1935, a tuberculin skin test (0.01 mg.) was negative at forty-eight hours. After that he was followed by the cardiac clinic, except for eight years when he was too well to return. Roentgen studies were made whenever the patient was available from



Fig. 3. Case II. D. D. Patient dying of rheumatic mitral heart disease, with autopsy diagnosis of pulmonary siderofibrosis. The nodules on the roentgenogram measure up to 3 mm. in diameter.

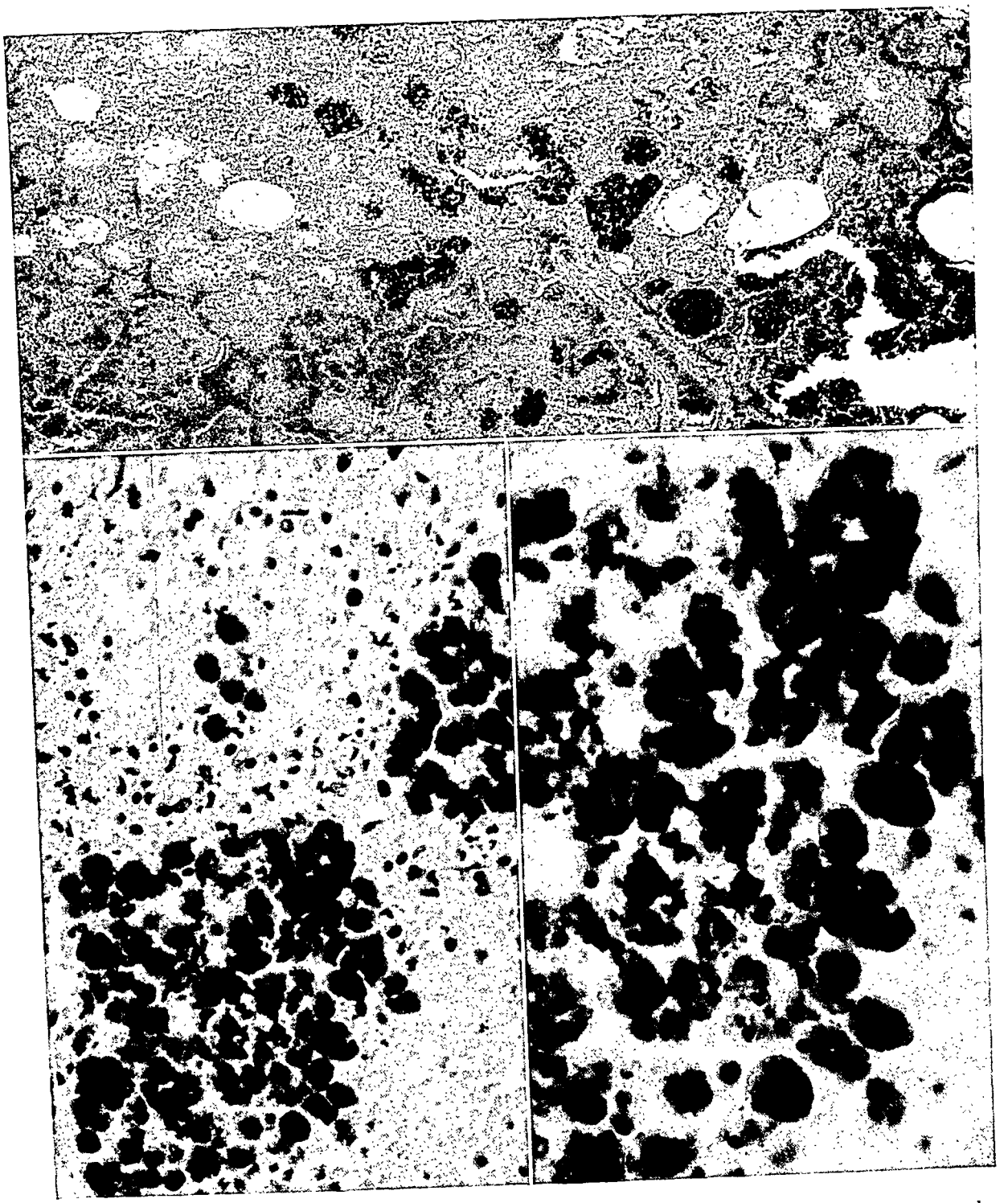


FIG. 4. Case II. D. D. Histopathologic details of lung showing siderofibrosis. Irregular clumps of macrophages containing hemosiderin, mostly intra-alveolar. Thickened septa and severe chronic passive congestion. (Hemotoxylin and eosin, 35×, 400×, 950×.)

January, 1935, to December, 1947. Mitral stenosis and regurgitation without congestive signs were recorded in 1944. At that time we did an intracutaneous tuberculin test with 0.0001 mg. P.P.D. and found it positive at thirty-three and forty-eight hours. He has never been exposed to dust hazards. At the present he continues working, but has periodic dyspnea and slight weakness. This is interpreted as arising from his heart damage. Our

first diagnostic inquiry was directed toward rheumatic pneumonia, a much debated entity. However, we could find no basis in the literature or from consultation with Drs. Thomas McMillan and Charles Wolferth to warrant the conclusion that the nodulations were due to rheumatic pneumonia.

The roentgenograms (Fig. 1 and 2) reveal a nodular lesion, generalized in both lungs, observed from 1935 to 1947. On January 8, 1935, there was a bilateral pneumonia and a background of definite nodulation (portable machine, supine exposures). The next study shown was of July, 1935, when the pneumonia had cleared. It is not certain that the nodules have changed. On June 17, 1941, the nodules seem larger, but the roentgenogram is very high in contrast. The heart may be larger. On May 9, 1944, we see that there is confirmation of larger nodules, which are definitely more distinct than in 1935. The heart appears unchanged. In December, 1947, there is no change in the nodular character (since 1941), but the heart seems larger. In all studies the characteristic mitral configuration was apparent by both postero-anterior and lateral exposures. The patient is living.

Following this, 3 cases of rheumatic mitral disease that bore great similarity to Case 1 were found at the Philadelphia General Hospital. On these, Dr. William Ehrich very kindly uncovered what lung tissue had been saved and described for us the histopathologic details. Dr. Ehrich warns that the specimens studied are so small (since interest in this disease was not active at the time of necropsy) that they may not be representative of the entire lung. However, the histopathologic and roentgenologic character coincide strikingly with material found in the literature.

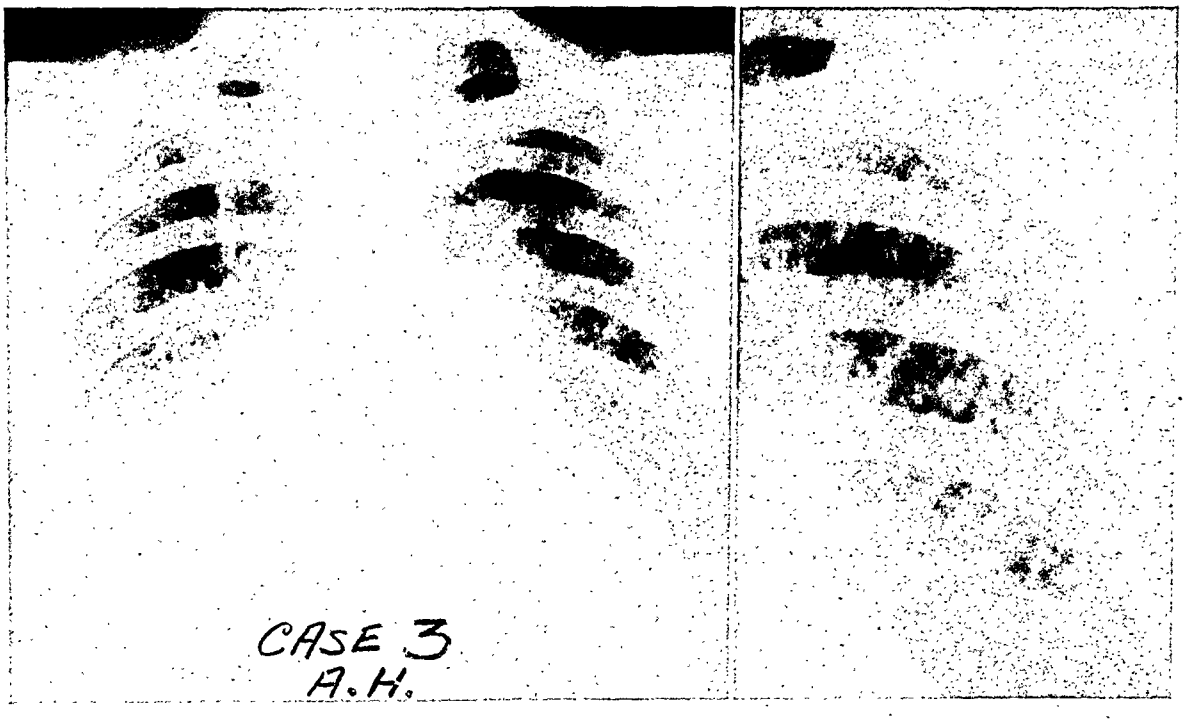


FIG. 5. Case III. A. H. Patient dying of rheumatic mitral disease with autopsy diagnosis of pulmonary hemosiderosis. The roentgen nodules measure up to 2.5 mm. and are seen easily on the original.

CASE II. D. D. (Fig. 3 and 4), male, white, aged fifty-eight. Rheumatic fever at the age of four. Shortly before final hospitalization he suffered recurrent ankle edema. Death occurred in decompensation.

The roentgenogram (Fig. 3) demonstrates marked nodulation, generalized, the nodules measuring up to 3 mm. in diameter. The heart indicates a double mitral lesion with marked ventricular hypertrophy.

Autopsy showed mitral and aortic stenosis

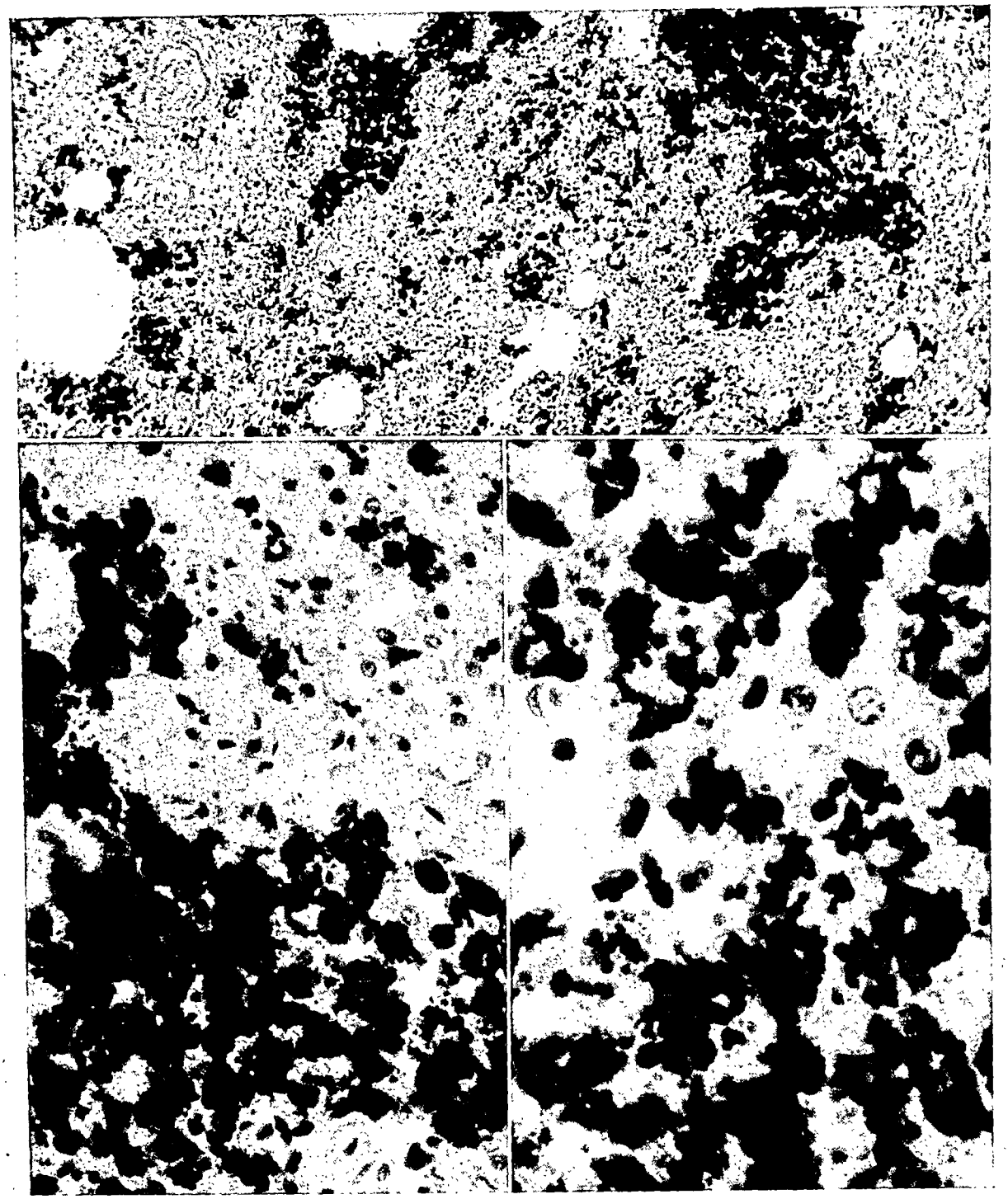


Fig. 6. Case III. A. H. Histopathologic details of lung showing hemosiderosis. Macrophages containing the pigment are intra-alveolar and interstitial. Nodules are 2 to 3 mm. in diameter but are of irregular outline. Hematoxylin and eosin with Prussian blue counter-stain, confirming the presence of iron. 100×, 400×, 950×.

and insufficiency (rheumatic) and myocardial hypertrophy. Histopathologic study of the lung reveals siderofibrosis. The slide contains hemosiderin collections large enough to be seen easily by the naked eye. Dr. Ehrich's description follows: Microscopic examination of the only piece of lung available reveals the picture of marked chronic passive congestion with siderofibrosis (Gamna-Gandy bodies). The capillaries are engorged with erythrocytes. The alveoli

contain numerous erythrocytes and some polymorphonuclear leukocytes. A portion of the alveoli is packed with macrophages containing large quantities of a yellow pigment, obviously hemosiderin. Some of the septa of the alveoli are thickened; the fibers composing the septa are rather straight in part and obviously incrusted with calcium. In other areas one finds round calcium clots as well as segmented yellow rods; the latter are mostly engulfed by foreign body giant cells. The pleura and the interstitial tissue show a good deal of coal pigment. There

Autopsy: Rheumatic mitral valvulitis, aortic and tricuspid valvulitis, dilatation of the left ventricle and hypertrophy of the right ventricle. Dr. Ehrich's description follows: Microscopic examination of the lungs reveals marked thickening of the septa, which are infiltrated with macrophages containing abundant blood pigment. The alveoli contain numerous densely crowded macrophages, mostly with much blood pigment, as well as proliferating bronchial epithelial cells, occasionally with mitotic figures. These various changes are definitely focal

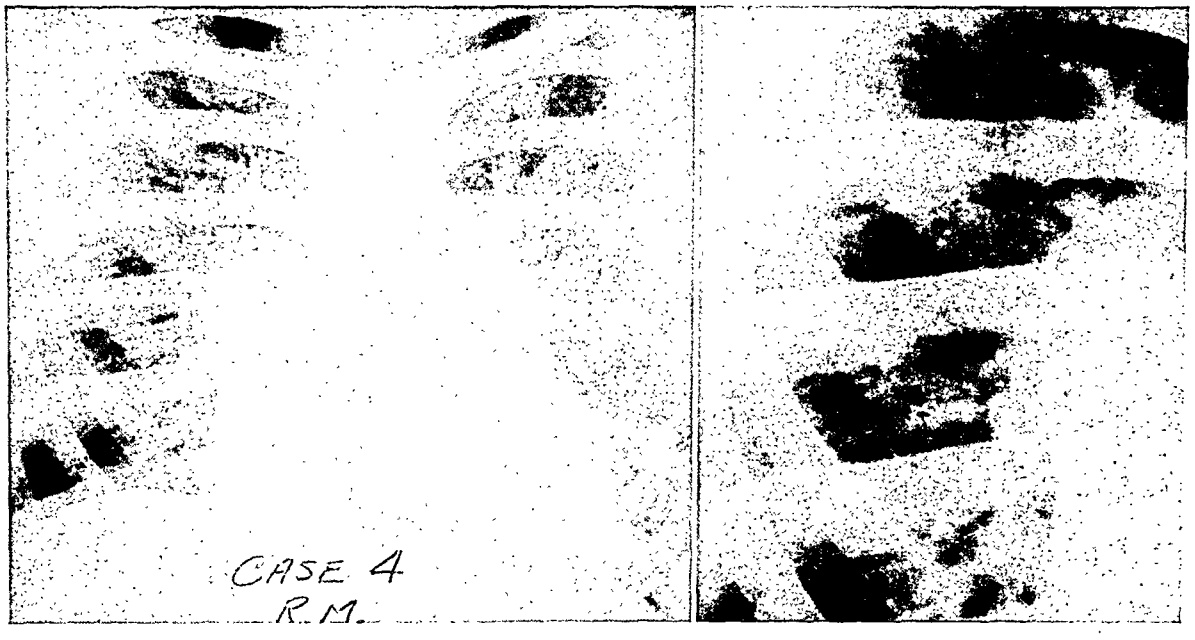


FIG. 7. Case IV. R. M. Patient dying of rheumatic mitral disease with autopsy diagnosis of pulmonary siderofibrosis. The nodules cannot be seen on the reproduction but measure up to 1.5 mm. on the original. Poor aggregation of iron is shown on the histopathologic slide.

are nodules measuring 1 cm. in diameter that are loaded with this pigment. Nothing suggests silicosis or asbestosis.

CASE III. A. H. (Fig. 5 and 6), female, white, aged thirty-five. No history of rheumatic fever. For six years there were increasing shortness of breath, fatigue and weight loss and more recently swelling of the legs and palpitation. On hospital admission there were bubbling and moist rales, a precordial bulge and thrill, a systolic mitral murmur and a presystolic slur. Electrocardiogram showed right axis deviation and inverted T waves. There was no response to digitalis and penicillin.

The roentgenogram (Fig. 5) reveals obvious small densities up to 2.5 mm. in diameter and a heart suggesting a double mitral lesion.

in character, causing poorly outlined nodules measuring 2 to 3 mm. in diameter. The pleura of the lung is thickened in some places and covered with a layer of fibrin. There is some infiltration with lymphocytes. The diagnosis is severe chronic passive congestion, fibrinous pleuritis and hemosiderosis (but no siderofibrosis).

CASE IV. R. M. (Fig. 7 and 8), male, white, aged twenty-four. The clinical history is not pertinent. The clinical diagnosis at death was rheumatic heart disease with auricular fibrillation and perhaps bacterial endocarditis; and epilepsy.

The only roentgenogram available (Fig. 7) shows very fine stippling in the upper two-thirds of the lungs, easily overlooked. The

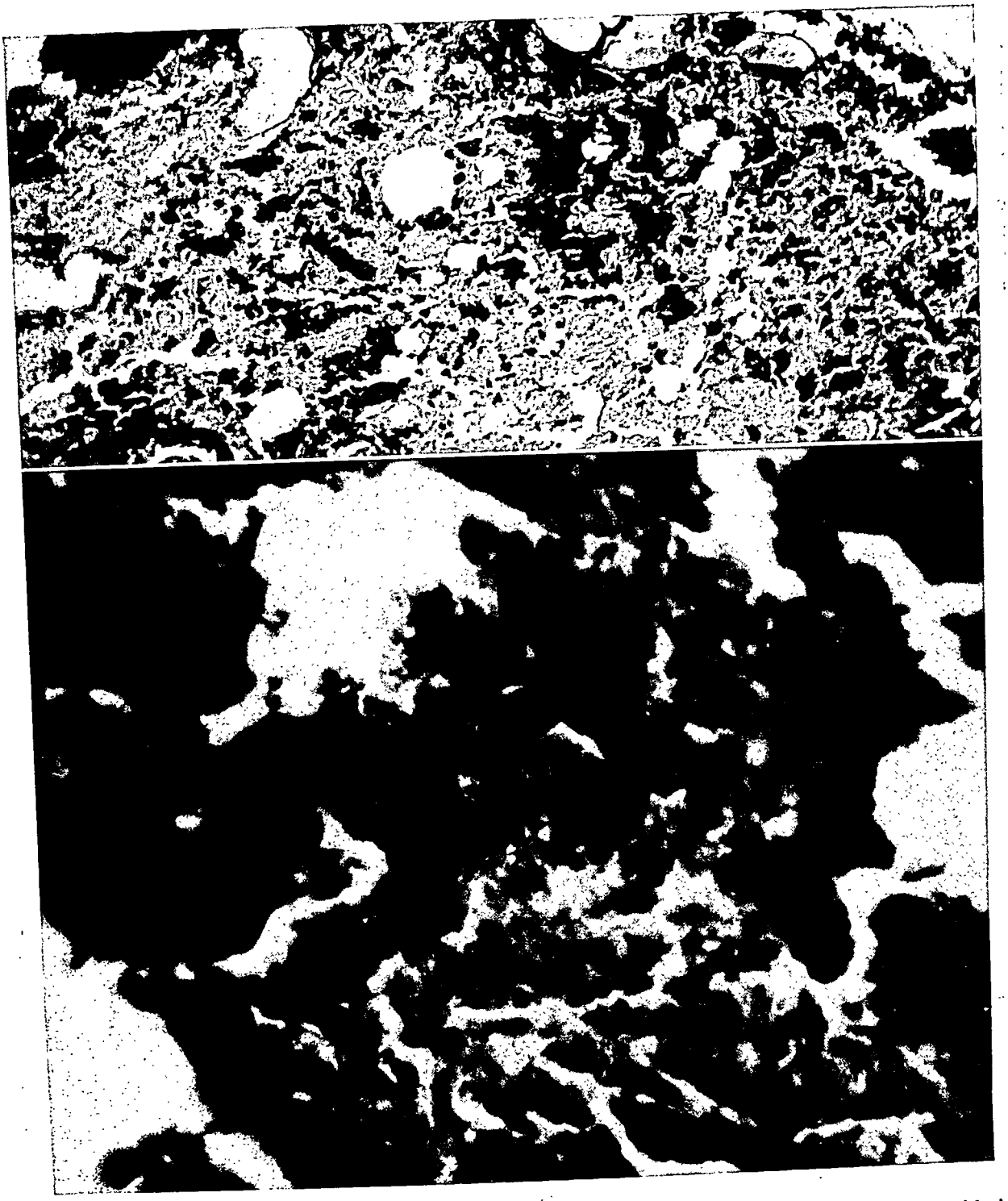


Fig. 8. Case iv. R. M. Histopathologic details of lung showing poorly defined collections of hemosiderin-laden macrophages and chronic passive congestion. Hematoxylin and eosin with Prussian blue counter-stain, confirming the presence of iron. 100×, 950×.

largest nodules measure 1.5 mm. and are very faint. The clumps of macrophages together with hemosiderin and fibrosis are hardly large and dense enough to cause roentgen nodules. The hemosiderin can be seen by the unaided eye on the tissue slide, but it is not well aggregated. The heart contour suggests a double mitral lesion, enlarged ventricles and a large pulmonary artery.

Autopsy: Dilatation and hypertrophy of both

ventricles and healed rheumatic mitral valvulitis. Dr. Ehrich's findings were as follows: The capillaries are engorged with erythrocytes. The alveoli are partly collapsed, while many are crowded with large numbers of macrophages filled with a yellow pigment, obviously hemosiderin. In the parenchyma of the lung as well as under the pleura one finds areas measuring 1 mm. in diameter where the macrophages are particularly numerous. Here the connective tissue reveals fibrosis and there are calcium incrustations of some of the fibers, as well as a few segmented yellow rods. There is nothing to suggest silicosis or asbestosis. The various sections of the lung available reveal the characteristic picture of chronic passive congestion with multiple areas of siderofibrosis.

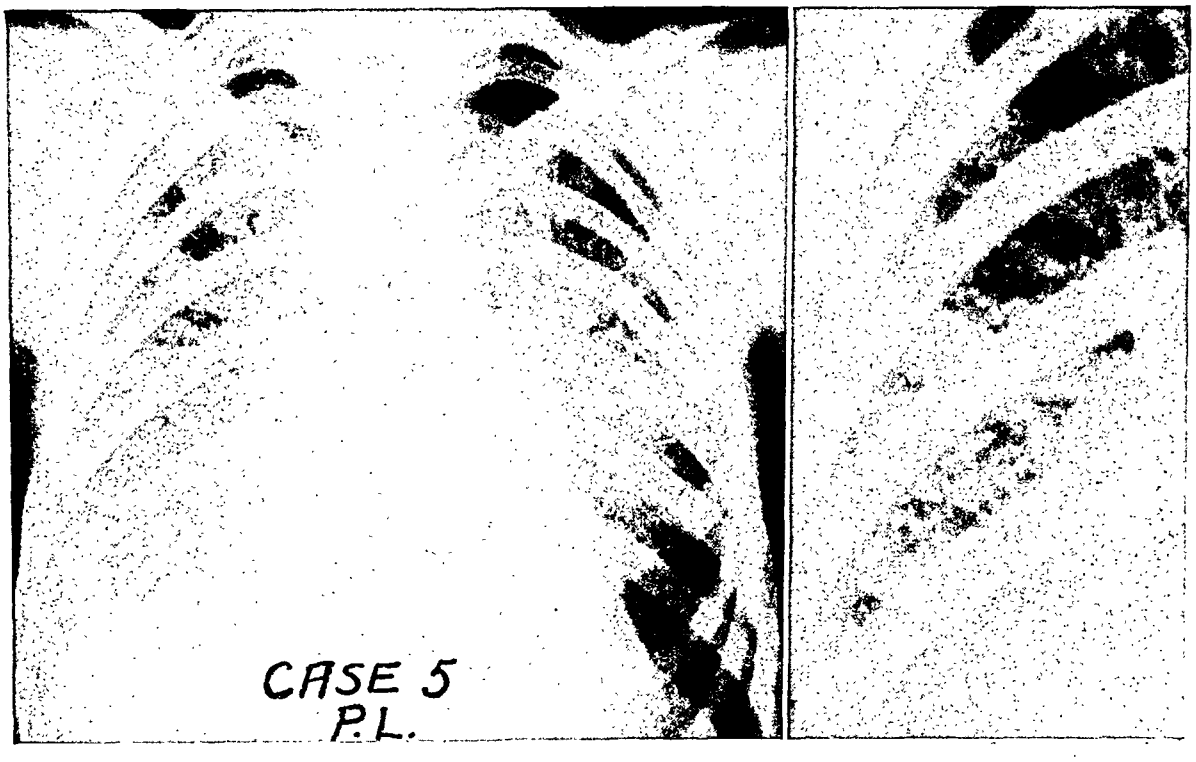


Fig. 9. Case v. P. L. (Case courtesy of Dr. Merrill C. Sosman.) Patient dying of rheumatic mitral disease with autopsy diagnosis of pulmonary hemosiderosis. Diffuse nodulation well seen on the original, but most of nodules are not over 1.5 mm. in diameter and not very dense.

Case v. P. L. (Fig. 9 and 10), male, aged twenty-four. (Generously provided by Dr. Merrill C. Sosman of Boston.) The patient had rheumatic fever at the age of four and was incapacitated by his heart from 1933 to 1934, when he was hospitalized with dyspnea and cyanosis. There were heart murmurs of aortic and mitral stenosis and insufficiency. Thoracentesis on the right repeatedly secured large amounts of fluid. Death occurred on the twenty-second hospital day.

Roentgenograms show a generalized fine nodulation in the lungs, together with moderate engorgement of vessels and a small amount of pleural effusion. The nodules are not over 1.5 mm. in diameter for the most part, but occasionally reach the size of 2 or 3 mm. On the tissue section they measure 1 mm., the discrepancy probably being due to multiple superimposition in the roentgenograms. The heart indicates enlargement of the pulmonary artery and the right ventricle.

Autopsy: Cardiac enlargement, adherent pericardium, stenosis of tricuspid, mitral and aortic valves and fibrinous vegetations on the free margins of aortic and mitral valves. The histopathologic lung findings as described by Dr. Ehrich are as follows: Edema and engorgement has created a thickening of alveolar walls, in some of which there is an inflammatory reaction consisting of fibroblast growth and infiltration by mononuclear and lymphoid cells.

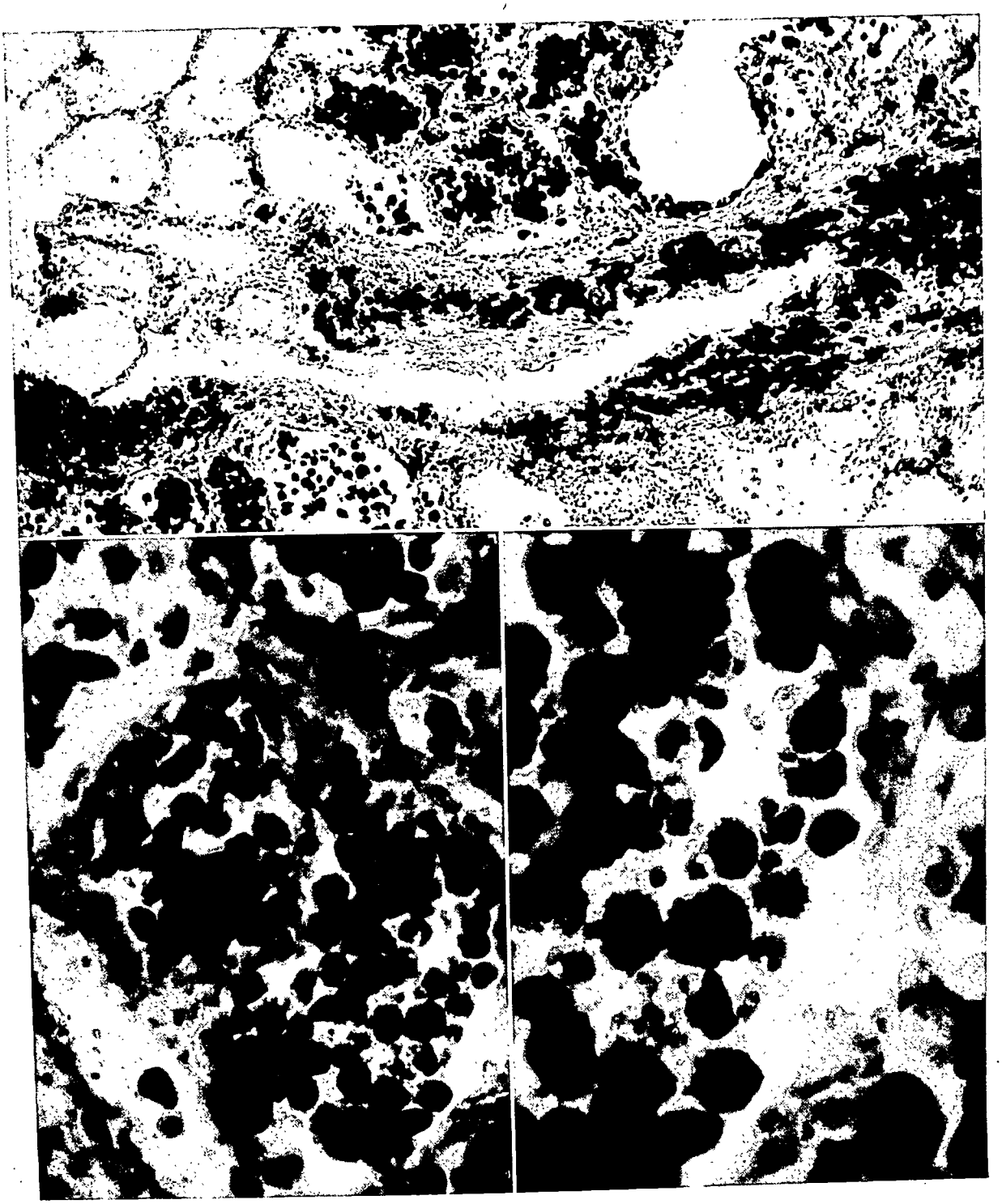


FIG. 10. Case v. P. L. (Case courtesy of Dr. Merrill C. Sosman). Histopathologic details of lung demonstrating chiefly alveolar but also interstitial location of hemosiderin-laden macrophages. The foci of iron-laden alveoli measure about 1 mm. in diameter. Hematoxylin and eosin with Prussian blue counter-stain, confirming the presence of iron. 100×, 400×, 950×.

There is intra-alveolar deposit of fibrin and leukocytes with transition to completely organized plugs. There are foci of alveoli, measuring about 1 mm. in diameter, that are filled with hemosiderin-laden macrophages. Histopathologic diagnosis: Chronic passive congestion with marked hemosiderosis and so-called rheumatic pneumonitis.

CASE VI. E. R. (Fig. 11), male, white, aged thirty-two. (Referred by Dr. J. Warren Hundley of Philadelphia.) The patient had rheumatic fever and diphtheria at the age of six. He felt well until 1944, when he noted shortness of breath, progressively increasing. Bed rest was necessary in August and October, 1947, for cough, fever and fatigue. There were recent night sweats, blood-streaked sputum and a characteristic rheumatic cardiac contour (including moderate left atrial enlargement), encouraged us in making this diagnosis after our acquaintance with the preceding 5 cases.

The patient was discharged to rest at home for six weeks prior to resuming light work. Follow-up visit one year later revealed no change in the pulmonary lesion, but an increased heart size and continued fatigue.

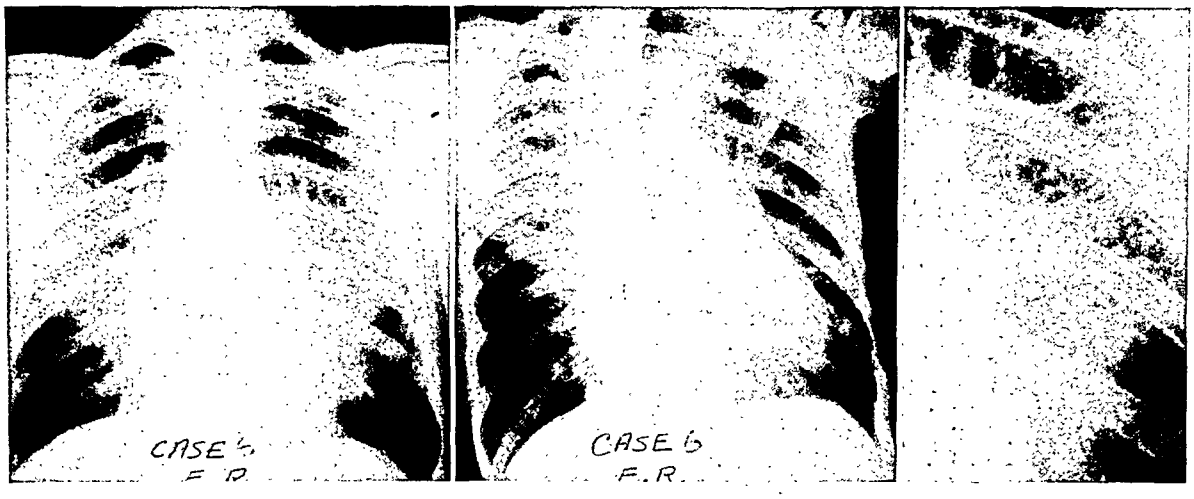


FIG. 11. Case VI. E. R. Patient living and working with mitral stenosis and insufficiency. Roentgen study elsewhere indicated miliary tuberculosis, but tuberculin skin tests and sputum-negative repeatedly. No change in the roentgenograms taken over a period of four months. A generalized nodular lesion just like that in the other cases is seen in all of this patient's studies.

fever of 102° F., which dropped abruptly under penicillin. No known exposure to tuberculosis exists. A chest roentgenogram elsewhere was diagnosed as miliary tuberculosis. He was admitted in December, 1947, with the following findings: Normal cardiac rhythm; a marked thrill at sixth interspace, palpable at both lung bases; a presystolic crescendo and faint systolic murmur at the apex and a short soft systolic murmur at the pulmonic area. There were wheezes in the upper lung areas and fine crepitant rales in the posterior and lateral bases. Old tuberculin skin tests were negative to 0.1 cc. of 1:100,000 and 0.1 cc. of 1:1,000. Three sputa and two gastric washings were negative for acid-fast bacilli. The temperature was normal and the blood culture negative. Clinical diagnosis: Rheumatic heart disease; mitral stenosis and insufficiency; cardiac enlargement.

Roentgen diagnosis on admission: Pulmonary hemosiderosis, secondary to rheumatic mitral disease. The generalized nodulation evenly distributed throughout both lungs, coupled with a

DISCUSSION

The 4 autopsied cases all show chronic passive congestion, some of which is severe. Two cases reveal hemosiderosis and two siderofibrosis. All histopathologic slides carry nodular aggregates that are visible by the naked eye and can be identified as areas of hemosiderin deposition. Three of the tissues have been stained with Prussian blue to confirm the diagnosis. The aggregates of iron pigment vary in size from 1 to 3 mm. in diameter. Apparently, not only the size but also the distribution and shape of the nodules governs the degree of roentgen visualization.

Thus, from the roentgen and microscopic study by other authors and ourselves it seems that *focal clumps* of hemosiderin and macrophages, with or without fibrosis and calcium deposition, can cause densities large enough to be seen on roentgenograms

of the lungs. This phenomenon occurs rarely in severe chronic passive congestion, in those dying of rheumatic mitral disease. It also occurs in mitral disease patients living comfortably without clinical evidence of congestion of the lungs. These persons may be supposed to be supporting a hemosiderosis with *inactive chronic passive congestion* (a phrase permitted by our colleagues in pathology). This is demonstrated by our 2 living cases and by the several living cases from New York[12] (although a different interpretation was placed on the latter by the reporting authors).

The presence of conglomerations of iron pigment makes these cases most interesting for comparison with the several groups, mentioned above, which have a similar, finely divided lung lesion, demonstrable roentgenographically. The cases of this report belong to the group of endogenous hemosiderosis, which includes the fatal anemias of children. The welders, rouge workers and metal grinders demonstrate the exogenous siderosis. Hemosiderosis of itself, as is true of pure siderosis, is a benign lesion, without attendant disability.

Carrying the roentgen diagnosis further, our cases would be problems to differentiate from the common pneumoconioses or miliary tuberculosis. The tell-tale evidence consists of the mitral configuration of the heart and the history of rheumatic valvular disease. A host of other diseases may and have been the subject of differential consideration. The following list is revealing:

Miliary tuberculosis	Bronchiolitis obliterans
Pneumoconiosis	Chronic passive congestion
Periarteritis	Polycythemia
Sarcoidosis	Brucellosis
Metastatic carcinoma	Tularemia
Histoplasmosis	Psittacosis
Ascaris infestation (?)	Leukemia
Aspergillosis	Hodgkin's disease
Bilharziasis	Lupus erythematosis
Bronchopneumonia	Xanthomatosis

SUMMARY

To the limited literature on pulmonary hemosiderosis due to mitral heart disease, we have added a report of four autopsied cases, and two living cases observed for several months and thirteen years respectively. In our findings there is confirmed the work of earlier (chiefly European) authors to the effect that this disease very rarely causes a deposition of hemosiderin in lung macrophages in sufficiently large clumps (1 to 3 mm. in diameter) to be recorded as a finely nodular roentgen density. This lesion must be differentiated from a host of diseases. A comparison is drawn between cases of endogenous hemosiderosis, exogenous siderosis due to iron dust, silicosis and miliary tuberculosis.

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DISCUSSION

Dr. George V. LeRoy, Chicago, Ill. I found this report very interesting indeed, and would like to congratulate the authors on calling to our attention yet another curious manifestation of rheumatic mitral disease. At the present time when mass roentgenography is gradually achieving its goal of an examination of the entire population it is well to appreciate the fact that a multiplicity of processes may yield a coarse nodulation throughout the lung fields. Most internists when confronted with films like the ones shown here would, I believe, be inclined to assume that their patient's rheumatic heart disease was complicated by some one of the serious conditions that Dr. Lame has cited in his list of differential diagnoses. Many of us, I am sure, would undertake as rigorous and complete a diagnostic study as possible, and even in the face of negative findings would be likely to take a fairly serious view of the roentgen findings. Recently, we had an elderly pa-

tient with congestive heart failure due to arteriosclerotic heart disease whose roentgenograms were similar to those we have seen today. He was examined repeatedly by several chest specialists, was bronchoscoped at least twice, underwent repeated gastric lavages and innumerable skin and sputum tests. At autopsy the lungs displayed chronic passive congestion and brown induration. It will be interesting to get the sections to determine whether hemosiderosis of the sort described was also present.

The importance of this report to clinicians consists, I believe, in the fact that the condition that is described is relatively benign when compared with most of the other causes of similar roentgen changes in the chest roentgenogram. The long duration of these findings in the first case—thirteen years—is evidence of this. The other clinical reports are too incomplete to permit an evaluation of this element; but I find it easy to believe that the lesions are harmless. Patients who display this sort of lesion must have some peculiar type of tissue reaction to the hemoglobin phagocyted in their alveoli, for it is certainly true that the majority of patients with rheumatic mitral disease have hemoptysis at one time or another, and most of them do not develop lesions of this sort.

I think it is not completely proper to group hemosiderosis and siderofibrosis with the so-called exogenous sideroses. The common feature of these three states is the presence of iron in the reacting tissue. In the forms of pneumoconiosis due to iron-laden dusts the size of the particles is probably critical. It is also of importance that the iron is in a metallic state, or in the form of an insoluble salt, as the oxide. The iron in hemosiderin forms a very small part of the molecule—less than 1 per cent—and under healthy conditions may be split off and returned to the body's iron pool. Likewise, with any deposit of hemosiderin there may be other iron-free residues of hemoglobin which have the same golden appearance in sections. The occurrence of calcification and ossification in the alveoli of patients with chronic congestive failure has been mentioned by many writers; and one is entitled to wonder how much of the shadows we see in these cases may be due to this phenomenon rather than to a reaction to the iron. The ease of the Prussian blue test may be misleading; and just because iron is present in such nodules is not adequate proof that iron caused them, in the sense that iron causes lesions in lungs of arc welders, for example.

Vol. 61, No. 4

THE APICAL FORM OF BRONCHOPULMONARY CANCER

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THIS is the most characteristic clinical form of bronchopulmonary cancer. Its primary development in the apex of the lung and, later, extension to the thoracic dome, is what gives it its nosological individuality and denomination as "cancer of the thoracopulmonary apex."

The site and growth of the tumor is characteristic, as this occurs in a region that forms part of the entrance to the thorax and is therefore crossed by important nerve elements whose alterations become exteriorized by typical symptoms, that, on being grouped together, constitute well known syndromes. The order of appearance of the symptoms is governed by the progressive development of the thoracopulmonary blastoma.

Though we say "bronchopulmonary," it should really be "bronchial," as our personal experience has proved it to be of bronchial origin, and not *branchial* or embryonal, as held by Pancoast when he speaks of them as "tumors of the sulcus pulmonaris superior." Neither have we been successful in encountering the metastatic forms due to neoplastic processes of other viscera, referred to by other authors.

After eighteen years of study of this clinical form of bronchopulmonary cancer, it is of special interest to note the regularity of the symptomatology and its appearance in definite stages, so that the development may be followed accurately to the end, as long as the evolution of the disease is not interrupted by death due to some intercurrent process.

The character of the symptoms and evolution of the localized neoplastic process in the thoracopulmonary apex amply justifies the opinion of the great Uruguayan physician, Dr. Ricaldoni, when he stated in 1918, "that there are more than enough reasons to group these lesions under a separate heading and that, in view of their mode of constitution, they should be called *irradiating lesions of the pleural dome.*" His masterly description of the symptoms that form this syndrome and his precise conception of the individuality of this pathological process have led us to give his name to this clinical form of cancer of the thoracopulmonary apex.

By so doing we are not overlooking Hare's important contribution when, in 1838, he described a patient who was suffering from "pains, prickliness and numbness along the ulnar nerve of the left arm, which were more pronounced in the elbow, where there was slight oedema and redness. There was also pain in his left scapula, but showed no physical signs on examination of the lung." The only possible source of this was a tumor found in the triangle on the left side of the neck, that according to Hare, "possibly compressed the origin of the branches of the brachial plexus."

Besides, Hare's patient also had left ocular signs, such as myosis and paralysis of the levator palpebrae superioris; these are mentioned in the case history, but with no comments.

His case, therefore, presented both the radicular and sympathetic symptoms and the tumor situated in the thoracic apex, but perhaps due to insufficient means of exploration, lacked the pulmonary apex symtoms.

However, it is impossible to speak of cancer of the thoracopulmonary apex without referring to the great American clinician and radiologist, Pancoast, and to his important contributions and the fundamental principles he laid down; these should be known to every practitioner, inasmuch as they enable us to reach a rapid diagnostic identification of the clinical form of this neoplastic process.

The important investigations carried out in Argentina, North America and Uruguay have brought this condition before the attention of the medical profession, while other American countries have also added valuable contributions; this has undoubtedly helped to stress the clinical and pathological individuality of this process, the knowledge of which is almost entirely due to the efforts of the medical science of our continent.

In a synoptic chart we have summarized the clinical evolution and main symptoms of this disease, and the syndromes that have been described up to the present.

We divide the evolution of cancer of the thoracopulmonary apex into four periods, as follows:

1st stage—onset
2nd stage—of extrapulmonary invasion
3rd stage—of characterization
4th stage—last period.

1. The *initial* period corresponds to the moment when the neoplastic lesion begins in the pulmonary apex and there are no physical nor functional symptoms, or if any, they pass unnoticed or they are attributed to another cause. A roentgenogram taken during this period shows a faint shadow in the apex of the lung; however, this very appearance is also found in cases of apical pleuritis, so we are deprived not only of the possibility of establishing an early diagnosis, but also of all the therapeutic advantages derived from it.

Perhaps bronchoscopy may, at some future date, enable us to discover the tumor in its intracanalicular initiation. Transthoracic puncture may also be attempted as a means of providing biopsy material.

2. *Extrapulmonary Invasion.* In its development the neoplastic lesion invades—either directly or by metastatic lymphangitis—the internal aspect of the greater supraclavicular fossa; that is to say, what is known as the thoracic apex; thus a single tumor mass is formed: that of the thoracic apex with that of the pulmonary apex. This tumor compresses all the structures lodged in the supra-retropleural fossa and its neighborhood; in other words, it affects the roots of the eighth cervical and first dorsal nerves and, at times, the stellate ganglion.

The compression of these nerve roots and their neoplastic infiltration brings about a radiculitis of the inferior brachial plexus, which is clinically shown externalized by pains of dull onset, that later become unbearable and resistant to all treatment.

It is at this stage that the patients begin a disheartening tour of hospitals, where they are usually treated for arthritis and many roentgenograms of the shoulder are taken, the results of which are negative, as can be expected. Others are considered cases of rheumatic neuritis and undergo all sorts of treatments, among which diathermy, short-wave therapy and ionophoresis are not omitted.

A knowledge that a radiculitis can be the result of an apical cancer should lead to a roentgenogram of the thorax in the presence of pain in the shoulder and the inner aspect of the arm. It is to Pancoast that we owe this important step that guides us to a correct diagnosis, inasmuch as on finding an apical shadow in the lung of a patient suffering from inferior brachial radiculitis and, much more so if there is already a shadow in the thoracic apex, it can be established that the cause is a cancer of the thoracopulmonary apex.

Having found the two clinical elements which constitute the *thoracic syndrome* of Castex, Palacio and Massei—viz., inferior brachial radiculitis and a roentgenographic thoracopulmonary shadow—it is possible to establish a fairly early diagnosis of cancer of the thoracopulmonary apex.

The speed with which blastoma invades the sympathetic fibers is manifested by the early or late appearance of oculopupillary and facial vasomotor symptoms, that may become evident during this period or appear in the following one.

3. *The Characterization Period.* It is during this stage that all the signs and symptoms appear which characterize this clinical picture.

They are, in order of appearance: (1) The *roentgen shadow of the apex.* (2) *Radicular pains of the inferior brachial plexus,* accompanied by hypotrophy or atrophy of the muscles receiving their nerve supply from the eighth cervical and first dorsal; besides, there is a slight, but evident reduction of their active movements. Inferior brachial paralysis which, associated with (3) the *sympathetic paralysis,* that is either limited to the ocular globe or affects also the communicant-rami 2, 3, etc.—established by redness and perspiration of the right side of the face—constitute *Dejerine-Klumke's* syndrome. (4) Sometimes there is a *phrenic paralysis,* which gives clinical signs of a pseudopleural effusion and roentgenologically shows a homolateral *hemidiaphragm elevation.* The phrenic symptoms may be associated with a paralysis of the recurrent nerve, especially when the blastoma is situated in the left side; in this case there may be present anginoid disorders that, associated with the earlier symptoms, constitute *Pardal's anginous form of cancer of the thoracopulmonary apex.* (5) At a certain stage of the disease, the study of serial roentgenograms reveals signs of *osteolysis,* which is a typical sign of the malignancy of the process. They also show how the apical shadow can either remain within its former boundaries or has invaded neighboring zones, thus becoming pseudolobar or lobar, according to whether it occupies part or the whole of the upper lobe of the lung. (6) The extrapulmonary progress of the process is shown clinically and roentgenologically by supraclavicular and supra- and infraspinous bulgings. These *bulgings,* as we termed them in our first publication on the subject in 1928, constitute the "paravertebral tumor" that, along with the nervous (radicular and sympathetic) and the apical symptoms, form part of *Tobias' painful apicocostovertebral syndrome.*

The diagnosis is easy in this third period, as all the signs and symptoms are present: a satisfactory testimony to the exactness of the diagnosis of a process that can no longer be modified, and that will shortly be confirmed by necropsy.

A further confirmation of the malignancy can be made through a biopsy of the tumor and either dyeing an extension of the material (Pavlovsky) or embedding it in paraffin, as we have done several times with our co-worker, Dr. Prado.

The disease pursues its relentless course and, before death, the patient enters the fourth and last stage.

4. The *last stage* is a result of the inward progression of the growth, which eventually reaches the spine and destroys the vertebrae. This destruction brings about a compression of the spinal cord through the meninges and a crural paraplegia, with exaggerated tendinous reflexes, Babinski's sign, hypertony, cell-albumin dissociation in the spinal fluid and sphincter disorders; moreover, there is anesthesia and trophic alterations in the zones situated below the pressure, the localization of which can be made exactly through Sicard and Forestier's method.

The ceaseless progression of the tumor is not hindered by the meningeal barrier, so eventually the cord is affected in such a manner that the spasticity of the limbs turns into flaccidity, with all the characteristics of a section of the cord.

In our first observation—published in 1928 with the pathologist, Dr. Bianchi—we pointed out the correlation between compression of the cord and cancer of the lung. In later papers we were able to confirm this from the clinical standpoint; furthermore, this assertion was afterwards supported by both Argentine and foreign sources. All this allows us to repeat here what we stated in earlier papers, that is to say, *that paraplegia through compression of the spinal cord has been seen in the last stage of all our cases of cancer of the thoraco-*

pulmonary apex, and that this occurrence is always present unless the clinical evolution of the disease is interrupted by death at an earlier stage.

From the aforesaid we may conclude *that in most cases and provided an infection does not interfere in the evolution, cancer of the thoracopulmonary apex starts as an intracanalicular process in a small bronchus and always ends with compression of the spinal cord.*

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VOL. 61, No. 4

A CASE OF CARCINOSARCOMA OF THE ESOPHAGUS*

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THERE have been a small number of tumors of the esophagus reported consisting of a commingling of two apparently different cellular components, one of them carcinomatous and the other sarcomatous. The nature and origin of these tumors is obscure and some confusion has arisen concerning their characteristics. The discovery and surgical resection of a case belonging to this group among the esophageal tumors observed at the Presbyterian Hospital, New York, has prompted us to report it and review other comparable cases appearing in the literature in an attempt to add to what little knowledge exists concerning these uncommon neoplasms.

CASE REPORT

E. R. (Unit No. 784298), a Finnish female domestic, aged forty-six, was admitted to the Presbyterian Hospital in August, 1945, at which time her complaints were dysphagia and retrosternal pain of eight months' duration. The pain, which was at first associated only with food intake, gradually occurred spontaneously, was localized just to the left of the xiphoid and radiated into the subscapular region. Occasionally, it became severe enough to wake her. She took no medication but modified her diet to consist of semi-solid and liquid foods. The patient lost 53 pounds during this period.

Clinical Findings. Physical examination revealed a ruddy, plump female who appeared well developed and well nourished, with no grossly abnormal findings. The blood examination disclosed a hemoglobin of 11.6 grams, white blood count of 12,100, with 68 per cent polymorphonuclears, 28 per cent lymphocytes and 4 per cent eosinophiles. The plasma proteins were 7.4 grams per cent. Examination of the esophagus with barium demonstrated a polypoid filling defect in its lower third a few centimeters above the diaphragm (Fig. 1 and 2). The lesion measured about 4.0 by 5.0 cm. in diameter. The roentgenological impression was carcinoma. Esophagoscopy disclosed a polypoid tumor which was attached to the anterior wall of the lower end of the esophagus. A biopsy was obtained but proved to be inconclusive. The procedure was repeated and a more adequate biopsy was taken. The quick paraffin sections, the roentgenographic observation, and the clinical story all substantiated the diagnosis of carcinoma.



FIG. 1. August, 1945. Polypoid filling defect in lower third of the esophagus.

First Operation. In October, 1945, the lower third of the esophagus was resected through a left posterior thoracic approach. The tumor was remarkable grossly in that it could be felt to slide up and down within the esophageal lumen. The esophagus was distended by the intraluminal mass, but did not appear to be involved by the tumor and there was no evidence of metastasis. The cut end of the esophagus was anastomosed to the gastric fundus within the chest.

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Course. Her recovery was rapid and without incident. She was discharged on the nineteenth postoperative day eating normally without dysphagia.

Interval History. Two months postoperatively the patient was gaining weight, eating solid foods, and had no major complaints. Her only difficulty was a little postprandial epigastric fullness. Roentgen examination at this time revealed no evidence of recurrence of the neoplasm.

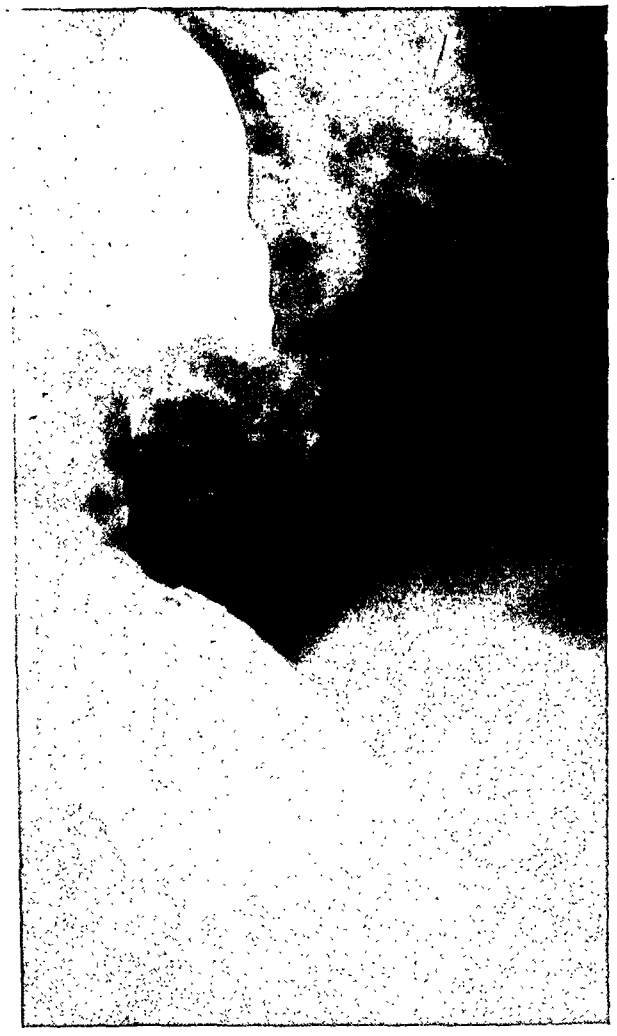


Fig. 2. August, 1945. Polypoid defect demonstrated in the lateral view.

In March, 1947 (sixteen months postoperatively) the patient complained of anorexia and slight weight loss, but had no dysphagia or chest pain. In May, 1947, hoarseness developed. A laryngoscopic examination showed complete lack of movement on the right of the arytenoid and vocal cord, with fixation of the latter. Roentgen study in June (Fig. 3), following recurrence of dysphagia, demonstrated a left anterolateral displacement of the esophagus at the level of the first and second thoracic vertebrae. The esophagus was slightly compressed and there was no delay in the passage of the barium. A roentgenogram of the chest showed slight widening of the right paratracheal shadow. The findings at this time suggested a mass extrinsic to the esophagus. Esophagoscopy disclosed an obstruction on the right, which was considered extrinsic at a distance 27 cm. from the upper teeth. No biopsy was taken as the mucous membrane appeared normal. The clinical findings suggested metastatic disease.

Second Operation. Because the unusual nature of the tumor suggested that it would resist radiation or nitrogen mustard therapy, and because it seemed possible that a single metastasis in the upper mediastinum existed which was causing symptoms by pressure rather than by direct extension and which might be sufficiently well encapsulated to permit removal, surgery was decided upon.

In July, 1947, the right upper mediastinum was approached transpleurally. A firm tumor mass about 3 by 4 cm. in diameter was found lying between the trachea and esophagus with its upper pole wedged behind the right subclavian artery and impinging on the recurrent laryngeal nerve. It was well encapsulated everywhere except behind the artery where it continued upward along the esophagus in intimate association with it. In this region tumor was cut across in excising the mass.

Course. Hoarseness and dysphagia were relieved, though not completely eliminated, for two months. In October a mass was noted in the right supraclavicular region. Soon thereafter she complained of dyspnea and cough, and tracheal compression was suspected. Dyspnea became progressively worse. Four doses of nitrogen mustard (0.1 mg. per kg. per day) were administered with only slight relief. Stridor persisted on both inspiration and expiration. The patient died in marked respiratory distress in November, 1947.

Pathology. The preliminary biopsies made were reported as from a malignant tumor but its true nature was not recognized and it was thought to be probably an anaplastic carcinoma.

The resected segment of esophagus measured 12 cm. in length and was somewhat sausage shaped with a maximum diameter of 5.5 cm. When the tube was opened, an ovate pedunculated firm tumor was seen with a smooth

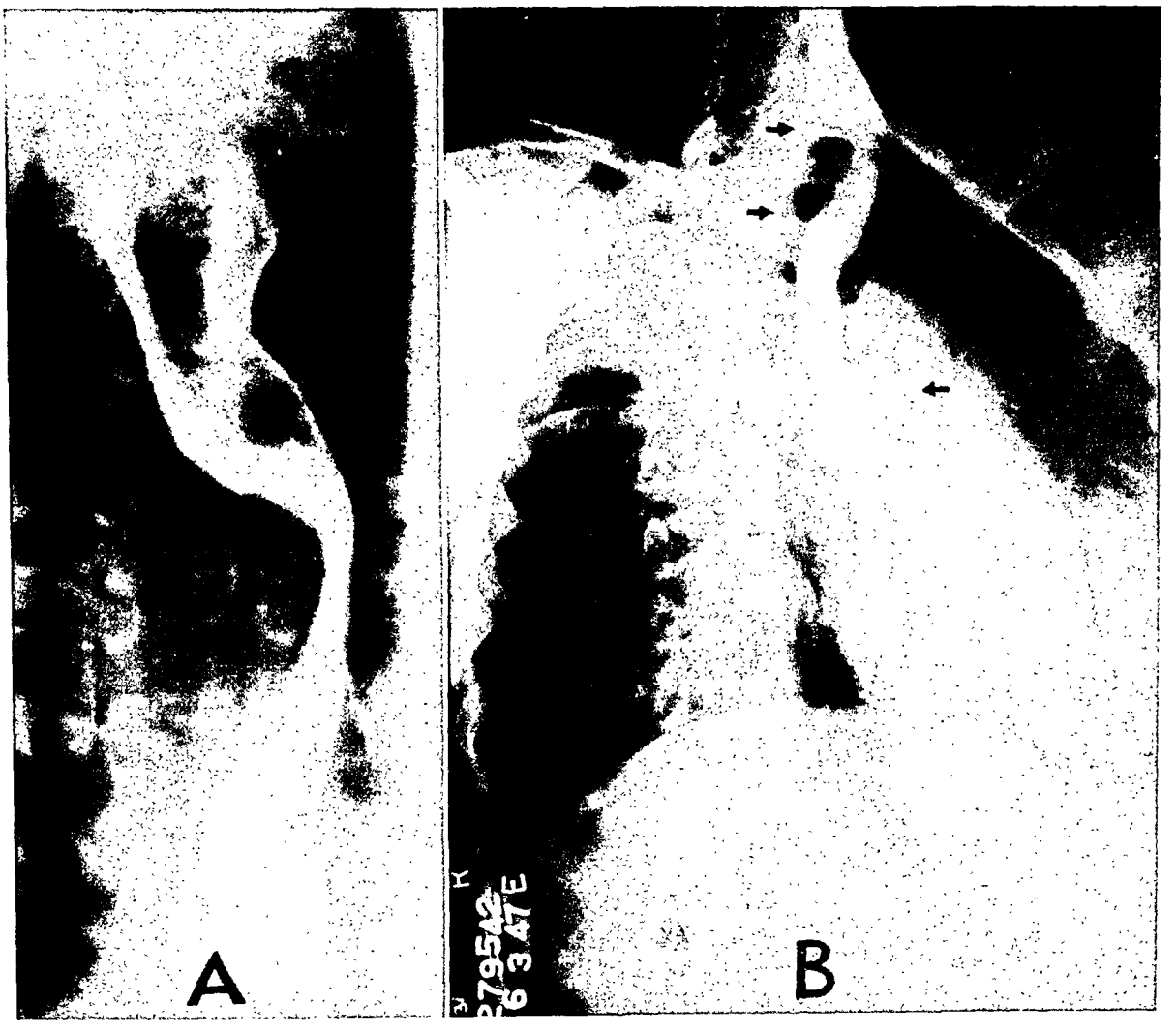


Fig. 3. June, 1947. An extrinsic mass in the right portion of the superior mediastinum displacing the esophagus anteriorly and to the left. *A*, anteroposterior spot roentgenogram of hypopharynx and upper esophagus demonstrating displacement of esophagus to the left. *B*, right anterior oblique projection. Upper arrows disclose anterior displacement of upper esophagus. Lower arrow at site of esophagogastric anastomosis.

slightly nodular surface covered with a grayish necrotic membrane. The over-all measurement was 9.5 by 5 cm. but the attachment to the wall only 6.5 by 1 cm. The cut surface of the growth was firm, pallid, and solid. It appeared to have only a superficial attachment to the esophageal wall (Fig. 4).

Microscopic examination in low power shows that the tumor has invaded the submucosa which is greatly thickened and exceedingly vascular but in no place has penetrated into the muscularis (Fig. 5). The tumor tissue is composed of two distinct elements; first, there are masses of undifferentiated epithelial cells most of which are found near the base of the neoplasm where it is attached to the esophageal wall but which occasionally can be detected also in the peripheral part, and second, the major portion of the tumor consists of a sarcomatous element which dominates the picture (Fig. 5). The epithelial cells are collected into masses outlined by a fibrous sheath. The individual cells are rounded, sometimes vacuolated, show no epidermoid differentiation nor any evidence of mucin secretion or tendency to form tubes or rosettes, and the individual cells are not infrequently separated by collagen fibers (Fig. 6). Nowhere do these cells of an epithelial habit seem to merge with the major bulk of the tumor which is made up of cells largely of spindle shape separated one from the other by a stroma rich in collagen and reticulin fibers in some places but much less so in others. These tumor cells vary enormously among

themselves from small to very large spindles and not infrequently giant forms appear which may be irregularly rounded with granular acidophilic and sometimes vacuolated cytoplasm and extremely bizarre nuclei. The general aspect of this sarcomatous portion suggests rhabdomyosarcoma although no proof of this is detected. Mitoses are very infrequent in the epithelial portions of the growth but common and often bizarre in the sarcomatous part (Fig. 6 and 7).

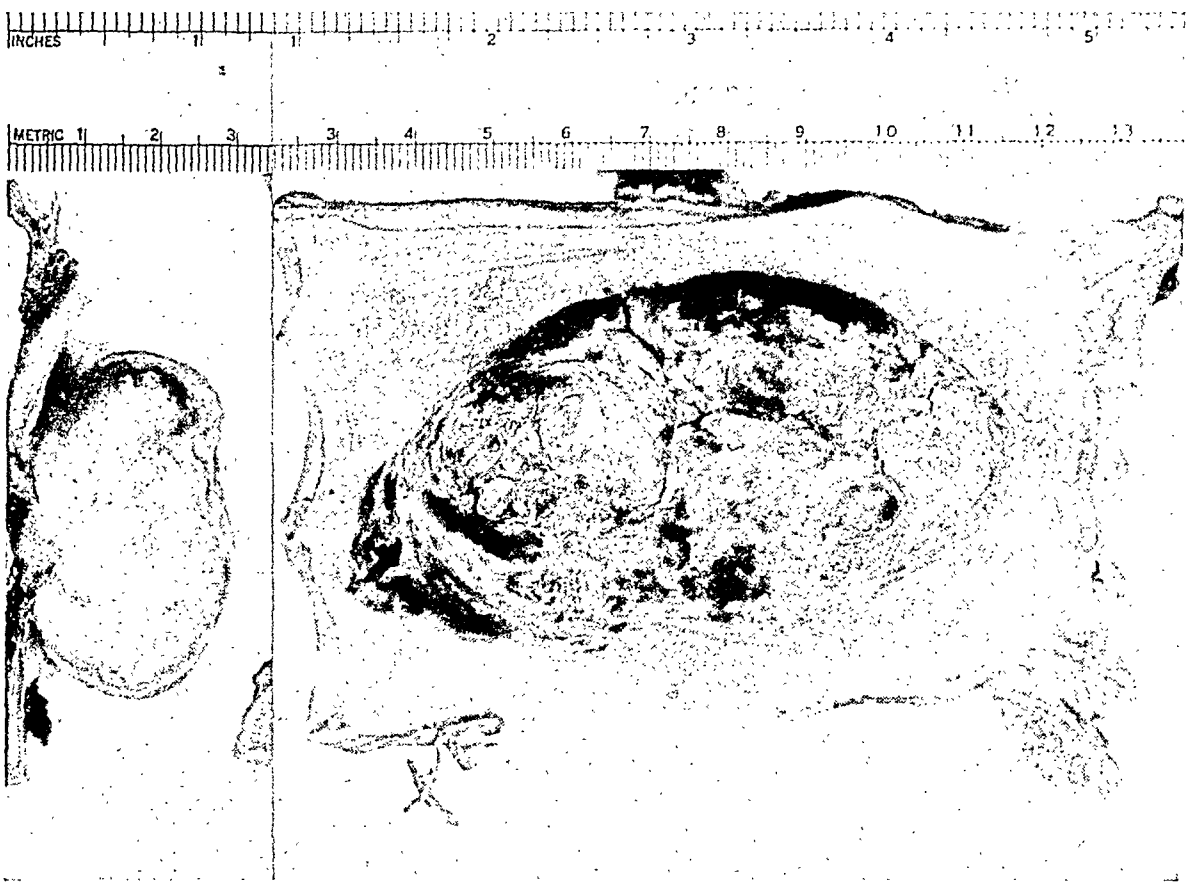


Fig. 4. Photograph of the opened esophagus showing the pedunculated tumor. At the left a cross section showing the pedicle and the absence of infiltration of the wall.

The spleen, which was removed, showed no unusual features.

The material removed at the second operation consists of small masses of tissue in which both lymph nodes and tumor tissue were recognized. Microscopically the metastatic tumor reproduces the sarcomatous elements of the primary growth. Although tumor tissue is found in close proximity to the nodes, no proof is obtained that the metastatic tumor tissue involves lymph nodes, although it is assumed that this is probably the case.

At autopsy (by Dr. Fletcher A. Miller of the Department of Pathology of the Presbyterian Hospital) a mass of tumor filled the upper mediastinum, grew into the esophagus from without, compressed the trachea and metastases were found in the superior mediastinal and right lower cervical lymph nodes but nowhere else (Fig. 8). The tumor microscopically at autopsy showed the same histopathology as was demonstrated at removal of the first metastatic mass: a reproduction of the sarcomatous elements of the tumor without any epithelial elements (Fig. 7).

COMMENT

The following are the important facts of this case. A pedunculated tumor developed on the anterior wall in the lower half of the esophagus of a forty-six year old woman, which produced a corresponding filling defect after barium was swallowed. The tumor was composed in part of a small number of undifferentiated epithelial elements, most of which were found near the base while the major portion of the growth had a sar-



Fig. 5. Low power photomicrograph showing the failure of the tumor to infiltrate the wall. The darker areas in the tumor near its base are epithelial cells.

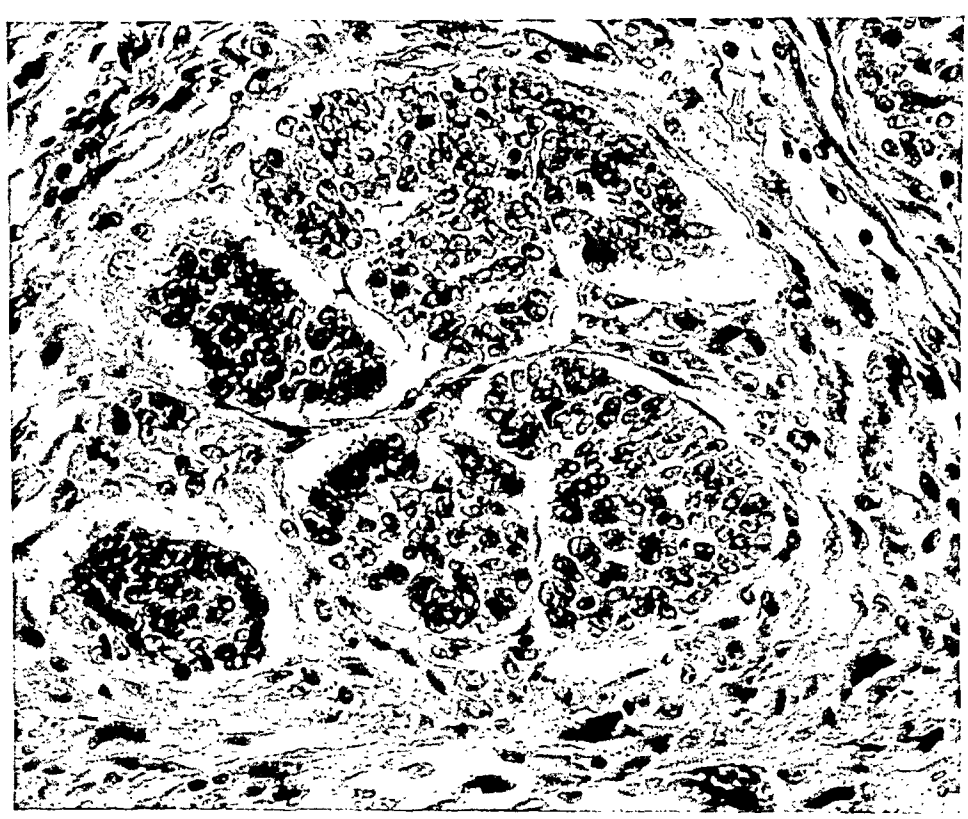


Fig. 6. Photomicrograph of groups of undifferentiated epithelial cells showing the absence of intimate relationship with the actively proliferating sarcomatous stroma.

comatous aspect suggesting rhabdomyosarcoma but without proof. Although limited to the mucosa and submucosa, it must have metastasized to the superior mediastinal nodes before its removal, although this was not appreciated at the time of operation. When these nodes enlarged an attempt to remove them failed and the persisting growth in the upper mediastinum eventually proved fatal. Except for the large recurrent mass which grew into the upper part of the esophagus, compressed the trachea and involved the right lower cervical and upper mediastinal lymph nodes, no other tumor was found at necropsy.

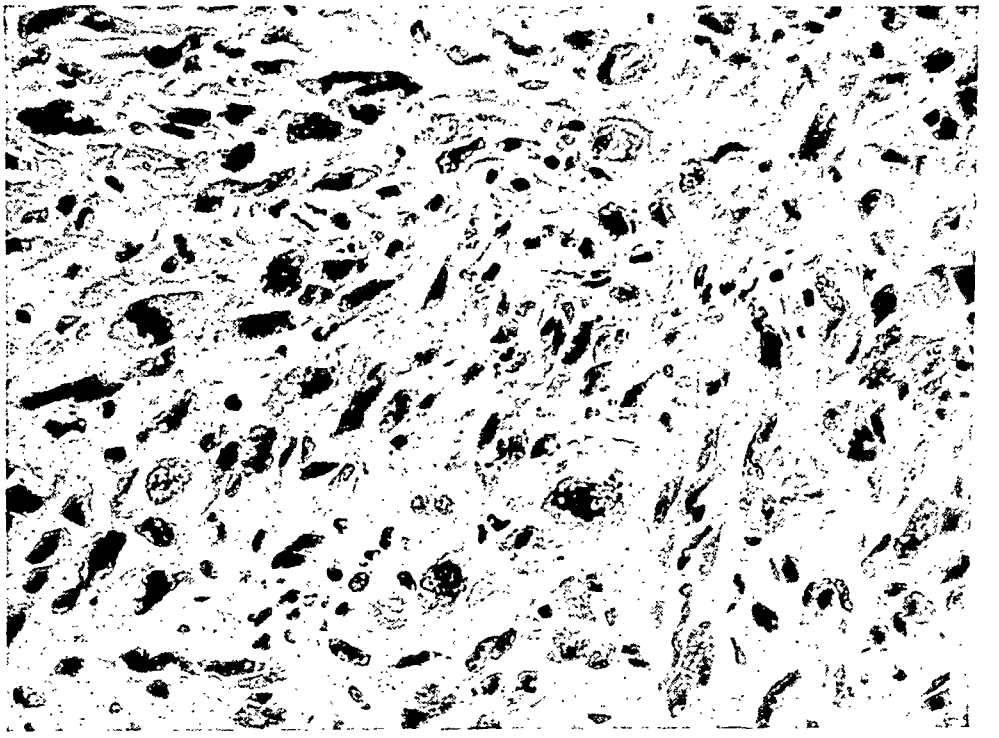


FIG. 7. Photomicrograph of metastatic tumor tissue at autopsy. The bizarre giant cells were found also in the sarcomatous part of the primary tumor.

There are reports of 10 other neoplasms which show a marked resemblance to this case. They are listed in Table 1A. They were all polypoid tumors. None was resected and all were studied at autopsy. Nine patients were males and one a female. All of the patients whose ages are recorded were forty-nine or more years of age and in every case but one the tumor was in the lower half of the esophagus. Metastases were present in 3 patients and 5 showed no metastases. In the cases of Cilotti, Heilmann, Kutsukake, Lang, Resch, and Harvey and Hamilton the epithelial tumor cells were called squamous; in the reports of Herxheimer and of Scarff this point is not clear and in Sokolow's tumor the epithelial cells were adenomatous. In all, the epithelial elements were deeply situated and the sarcomatous cells included spindle shapes and usually giant forms. The metastases of the 3 cases in which these were found consisted only of sarcomatous elements.

Ten other cases in which what are described as both epithelial and mesodermal cells were found have been included in the same table. Kinoshita's patient had a polypoid tumor in the upper esophagus at the level of the cricoid cartilage which included cartilage and myxoid elements as well as epithelial strands and sarcomatous areas. This seems to be more in the nature of a true teratoma. Cases 12 to 18 are all nonpolypoid infiltrating tumors occurring in various parts of the esophagus of elderly

men and women. In all of the cases except those of Blackburn and of Socin, the authors describe the epithelial tumor cells as squamous. In these two there were undifferentiated epithelial tumor cells. Three cases had metastases. Those from the man. None of these authors has studied personal cases and they suggest that the histopathological appearance is simply a manifestation of metaplasia occurring in squamous cell cancers of the esophagus. It is not possible, of course, to disprove this

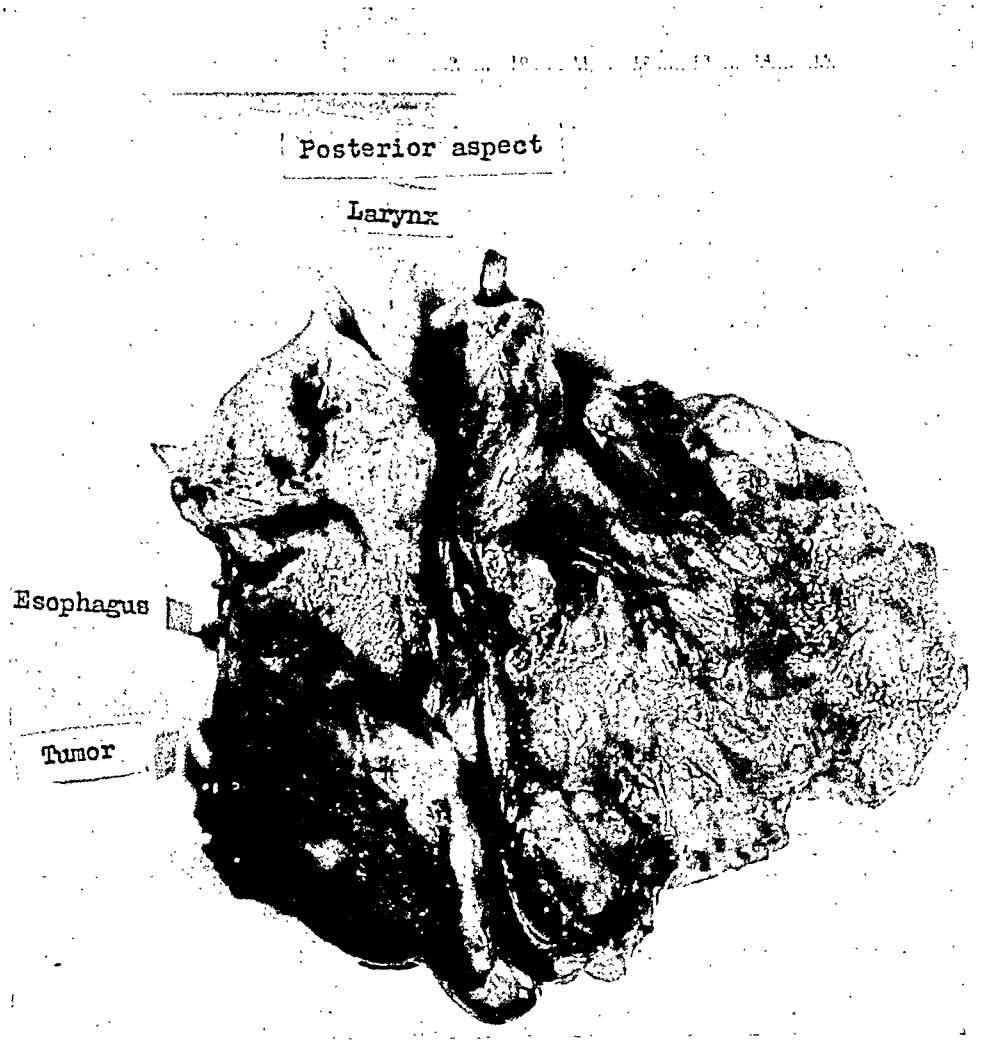


Fig. 8. Photograph showing tissues removed at autopsy. A large tumor mass projects into the opened esophagus ("tumor") and the trachea is surrounded by tumor.

tumors described by Donath and by Herzog reproduced the appearance of the primary tumor. Kahlstorf's patient showed spindle cells only in the metastases.

There seems to have been a dearth of reports of such mixed tissue tumors in recent years since the development of the operation of esophagectomy. Perhaps, because of this scarcity, doubt of the essentially dual nature of these neoplasms has been expressed by Saphir and Vass and by Pearl-

hypothesis but if true it does not invalidate the observation that the tumors represented by the present one and the 10 others resembling it in Table 1A are quite different from the ordinary esophageal cancer, which is not polypoid, infiltrates the esophageal wall quite freely, metastasizes in 69 per cent of cases (Klein) and is seldom cured. Judging from the fact that only 3 of the 10 neoplasms recorded in Table 1A are known to have metastasized, one would

TABLE I

CASES OF "CARCINOSARCOMA" OF THE ESOPHAGUS

	Sex	Age	Size	Metastases
(A) *Polypoid Growths with Epithelial Elements at the Base, Sarcomatous Elements Throughout and no Epithelial Elements in the Metastases*				
1. Cilotti	Male	75	Almond	Liver, pancreas, lung, pleura, 2 ribs
2. Harvey and Hamilton	Male	49	?	No mention
3. Heilmann	Male	65	14 cm. long	None
4. Herxheimer (1918)	Male	73	6 cm.	None
5. Kutsukake	Male	51	11 cm.	Regional nodes
6. Lang	Male	67	?	Liver, regional nodes
7. Lang	Male	52	Small	None
8. Resch	Male	74	10×5×5 cm.	None
9. Scarff	Male	50	$1\frac{1}{2}\times3\frac{1}{2}$ in.	None
10. Sokolow	Female	?	8×3 cm.	No mention
All of these cases were in the lower half of the esophagus, except that of Harvey and Hamilton which was hypopharyngeal.				
(B) *With Cartilaginous Elements as Well*				
11. Kinoshita	Male	58	?	None
(C) *Infiltrating, Non-polyploid Growths with Epithelial and Sarcomatous Elements Diffusely Intermingled*				
12. Blackburn	Female	53	Large	No mention
13. Bösenberg	Male	56	Large	No mention
14. Donath	Male	52	Large	Regional nodes
15. Herxheimer (1908)	Male	67	11 cm.	No mention
16. Herzog	Female	80	Large	Liver and regional nodes
17. Kahlstorf	Male	42	Large	Widespread, including bones
18. Socin	Female	60	Large (in diverticulum)	No mention
(D) *Cases Mentioned without Details*				
19. Carnevale-Ricci				
20. Hansemann				

anticipate that several of these patients might have been cured had a partial esophagectomy been done.

As for the cellular origin of this tumor we have only speculations to offer. Sections of it were studied by Pierre Masson of Montreal who suggested its resemblance in some respects to the carcinosarcomas of the breasts of bitches and human females which he supposes have a common origin from epithelial elements and which differentiate in two directions both as carcinomas and sarcomas, forming what R. Meyer would call a combination tumor. In the case of this tumor Masson suggests an esophageal mucous gland as the possible source. This explanation may be correct; we have no constructive thoughts about it other than it represents an entity which differs not only grossly and microscopically but also in its biological behavior and roentgenological aspects from the usual esophageal cancer.

SUMMARY

A case of pedunculated carcinosarcoma of the esophagus is reported. The roentgen findings are illustrated in detail. After resection of the esophagus, mediastinal metastases manifested themselves. An attempt to remove all of these failed and the patient eventually died with secondary invasion of the esophagus and metastases in the mediastinum and lower cervical nodes.

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MASS ROENTGENOLOGICAL SURVEY OF THE GASTROINTESTINAL TRACT TO DETECT CANCER OF THE STOMACH

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MASS roentgenological surveys of the chest have been widely accepted as valuable methods for detecting pulmonary disease in presumably normal individuals. These surveys had wide usage in the armed forces of many countries in World War II and are now being extended to civilian life.

There are glaring defects in mass chest roentgenological examination which are commonly overlooked: first, there is the possibility of detecting more cases of pulmonary disease than there are facilities for caring for them; and second, overemphasis on the value of roentgenological methods in finding pulmonary disease at the expense of other methods of making a diagnosis, such as history, physical examination, weight charts, temperature charts, and so forth. It is indeed strange that eradication of the tuberculous food animal (as done by the veterinary inspectors of the Federal and State Bureaus of Animal Industry) is enormously successful and has diminished greatly the incidence of tuberculosis in domestic animals. These inspections have been in a sense mass surveys, but there was no resort to miniature roentgenograms.

Mass roentgenological survey to detect gastric cancer is being thought of fairly widely. Funds have been requested from both government and private sources for this type of survey. It is generally accepted that gastric cancer is the most frequent cause of cancer deaths, greatly exceeding that of any other organ or tissue. It is also widely and rightly believed that, given a sufficiently early diagnosis of gastric cancer, the outlook for cure by surgical intervention is good. Cancer of the stomach can be so insidious, however, that it is beyond any form of treatment when discovered. This is due to the absence of any symptoms or manifestations that would lead to examination of the patient either by the roentgen ray or any other means. Some great physicians and surgeons, while seemingly in perfect health, have had the diagnosis of gastric cancer made only when the disease was in a hopelessly advanced stage. One noted surgeon made the diagnosis when he felt the lump in his epigastrium while bending over the operating table! Indeed, it would be a wonderful thing if mass gastric roentgenologic surveys on well individuals could be successfully employed. It could, if found feasible, save many lives.

However, statistics on cancer and cancer deaths indicate that the high incidence of gastric cancer is exaggerated and more and more cancer of the other segments of the gastrointestinal tract and also of other regions of the body are being found more frequently. The Connecticut State figures (where cancer is reportable) for the relative occurrence of cancer of the alimentary tract are as follows per 100,000 population:

Esophagus	3.2
Stomach	15.6
Rectum	10.8
Colon	9.25
Small intestine	0.6

(1940–1946)

The only publication on mass gastric surveys to be found at the time of writing is that of Swenson.[3] He states that any great mass of people examined roentgenoscopically alone would require far more radiologists than are available for that

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purpose. Of course, using the roentgenoscopic method is a very uncertain way of detecting any early lesion. Those that would be obvious in a rapid survey with the roentgenoscope would generally be too far advanced for any sort of successful treatment; also, there would be enormous risk to the roentgenoscopist. As in mass surveys of the chest, it is the early lesion that is most likely to be overlooked by any sort of roentgen examination, and it is the early lesions for which most can be done.

At the 1947 meeting of the American Roentgen Ray Society, Kirklin and Hodgson,[1] in discussing mass gastrointestinal roentgenological surveys, demonstrated that it would be necessary to examine individuals every three months, which, for the whole adult population of the country, is an absurdity. Rigler[2] examined 544 individuals over the age of fifty, symptomless except for a low acidity or aclorhydria. He discovered by roentgen examination 3 cases of gastric carcinoma, which were found by operation. He stated that there was one case which was missed through "an error in interpretation." In his group he had 11 other cases that did have gastric carcinoma, but they were not to be considered because they were not symptomless.

To appraise critically the value of mass gastric surveys, three points will be considered:

1. The relative incidence of cancer of the alimentary tract in its several segments, as discovered by the roentgenographic method.
2. The efficiency of the opaque meal roentgen examination in detecting early cancer of the gastrointestinal tract.
3. Its numerical relationship to the number of cancers seen in a general hospital roentgen-ray department.

There are available for study of these points 30,985 examinations of the gastrointestinal tract from the years 1916 to 1947, inclusive. The method of examination, recording, and reporting was that which originated with the late Dr. Russell D. Carman and the late Dr. R. Walter Mills, and their plan has been consistently followed since with carefully annotated records.

Gastrointestinal examinations were complete in 69.6 per cent and incomplete in 30.4 per cent of the cases. A complete gastrointestinal examination consists of examining the entire tract from the esophagus downward. The oral and pharyngeal cavities and the anus are not included. The examinations were made by giving the opaque meal and watching its progress throughout the entire tract. A barium enema is included and since 1924 cholecystography has been a routine procedure. The patient is first scanned with the roentgenoscope and any findings noted. In the preliminary survey the positioning for the ensuing films, which are always made, is decided upon. The opaque meal is administered and the patient is roentgenoscoped in both the supine and erect positions, and in as many directions as seems advisable to the roentgenoscopist. As many roentgenograms are taken as are considered necessary in all cases. The function of the roentgenoscope in this material has been that of an instrument for the advantageous taking of roentgenograms. This is laborious and requires time, regardless of how expeditious and skillful the examiner may be. There are: a first examination, a five hour observation, a twenty-four hour observation, and at forty-eight hours, the opaque enema after evacuation of residual barium meal is given; on the same day, cholecystography is done. In incomplete examinations, some part of the preceding is omitted as a matter, perhaps, of economy in time or failure of the patient to return. Occasionally when the esophagus is suspect that structure only would be examined. But the effort has always been to make a complete study throughout the tract. In case of any ambiguity, any part or all of the procedure was repeated.

The roentgen diagnosis of carcinoma of the gastrointestinal tract was made in 1,352 of a total of 14,337 pathological cases.

GASTRO-INTESTINAL EXAMINATIONS--1916-1947

Gastro-intestinal Examinations - complete	69.6%)	
	)	30,985
Gastro-intestinal Examinations - incomplete	30.4%)	

CARCINOMA OF GASTRO-INTESTINAL TRACT (9.4%)

ESOPHAGUS	STOMACH	SMALL INTESTINE	COLON	RECTUM
252 (18.6%)	619 (45.8%)	3	367 (27.2%)	111 (8.2%)
	Confirmed--86%	Confirmed -- 66.6%	Confirmed--91%	Confirmed--75%

ULCERS

GASTRIC	DUODENAL	GASTRIC ULCER WITH ULCER OF DUODENUM
336	1,886	24

OTHER PATHOLOGICAL DIAGNOSES:	10,739	(34.7%)
CARCINOMA:	1,352	
ULCERS:	2,246	
	14,337	

Of the total gastro-intestinal examinations conducted during this period (30,985), it is readily seen that the percentage of pathological diagnoses (14,337) constitutes 46.3% while carcinoma constitutes 9.4% of the total of pathological cases.

Chart I

PERCENTAGE OF GASTRO-INTESTINAL CARCINOMATA IN MALES AND FEMALES

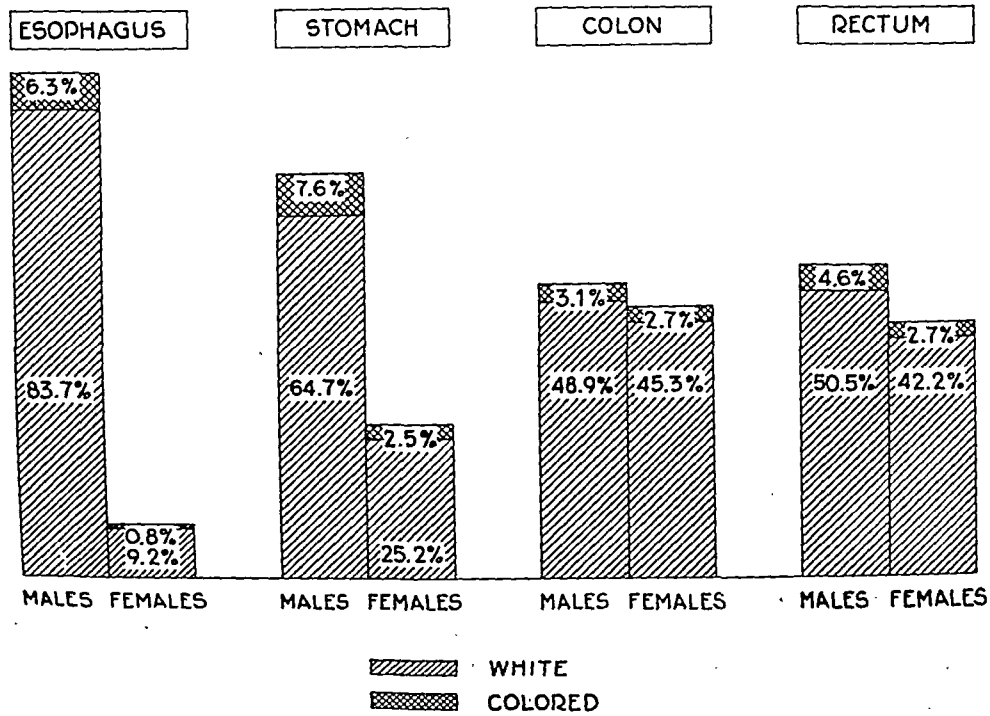


Chart II

The number of gastrointestinal examinations was 30,985, of which 46.3 per cent were of pathological import, and of these, 9.4 per cent were carcinoma.

The accompanying chart (Chart I) shows the number of cancers in the different segments of the gastrointestinal tract with the diagnoses confirmed either by autopsy, surgically, or endoscopically. The correctness of diagnosis in the case of the esophagus is unknown, but was very high. The accuracy of diagnoses elsewhere in the tract was high and shows a splendid efficiency for the roentgenographic method of examination.

In reviewing this material and considering the technique employed, it is apparent that the stomach will not lend itself to mass roentgenological surveys with any degree of success for many reasons. Among them is the time and labor required and risk involved. The fact that there is a high incidence of cancer in the other segments of the gastrointestinal tract is ignored. If all gastric cancers were diagnosed early by mass methods, there would remain a large number of cancers elsewhere in the tract that would escape detection. It must be remembered that this material was in a general hospital and practically all of the cases examined were patients with some symptoms ascribable to the alimentary tract; in other words, it is largely a pathological group; yet, the percentage of cancer is quite low. This material showed that 93 per cent of the patients studied were white. Chart II shows a relative incidence in the sexes. There is vast food for thought in the relative incidence of carcinoma of the esophagus and of the stomach in the sexes. Cancer of the colon and rectum are pretty close to the same incidence in the sexes. As to age, Chart III shows what would be anticipated—a tremendous incidence in the fifth and sixth decades.

The belief has been stated above that the frequency of cancer of the stomach is too high, particularly in relationship to cancer elsewhere in the body. Over approximately the same period which this survey covers there were 6,245 patients with cancer elsewhere in the body receiving radiation

DISTRIBUTION OF GASTRO-INTESTINAL CARCINOMATA ACCORDING TO DECADES

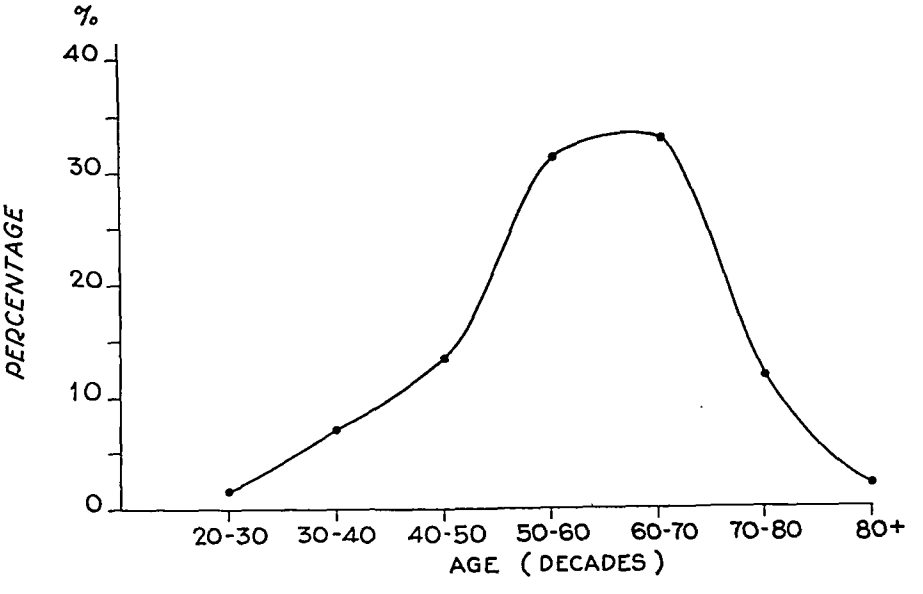


CHART III

treatment. These were grouped as follows:

Female genitalia	2,515
Breast	1,014
Skin	486
Male genitalia	477
Mouth	425
Upper respiratory tract	313
Genitourinary (both sexes)	291
Lungs	246
Skeleton	154
Lymph nodes	94
Miscellaneous	230

The roentgen-ray opinion of malignant tumor has been advanced in 2,625 diagnostic cases, exclusive of the gastrointestinal tract. In the diagnostic figures, there was present on roentgen examination of the lung 559 carcinomas of that organ. This does not include the metastatic tumors.

An astonishing fact is that in the thirty-one years covered by this study there have been but two correct roentgen diagnoses of carcinoma of the small intestine. In this same period in a total of 192,536 hospital admissions[4] there were only 7 additional small intestinal cancers. Only 2 had a correct preoperative roentgen diagnosis in this series, and 1 had the examination made elsewhere. There was 1 incorrect diagnosis —perforation of the duodenum, which was caused by a carcinoma. The remainder were found at autopsy or at surgical operation for obstruction or perforation. The incidence of the different portions of the small intestine was: 2 of the ileum, 3 of the jejunum, and 3 of the duodenum.

It seems safe to conclude that with the present state of the art of gastrointestinal examination it must still remain an art and is therefore not suitable for mechanization such as would be the case with mass survey film techniques. Although there might be some possibility of detecting cancer of the stomach with this method, it probably would detect only the late cases. The accepted method of examination by the radiologists of this country is highly efficient, and gastric cancer of the one type which seems to be suitable for detection by mass survey methods comprises but a small part of the malignancy problem and even a relatively small part of the incidence of gastrointestinal cancer.

From the data which have been accumulated, it is obvious that overemphasis has been placed on the incidence of cancer of the stomach. It is, of course, true that different data will be found in different clinics, but on the whole, sight must not be lost of the fact of the terrifically high rate of cancer of the female breast, the uterus, and the lungs.

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PARAPLEGIC NEUROARTHROPATHY*†

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THE purpose of this communication is to call attention to certain neuropathic articular and periarticular changes occurring in the lower extremities of paraplegics. Their condition, as is well known, is a paralysis of the lower half of the body due to disease or injury of the spinal cord. This discussion concerns itself primarily with cases of transection of the cord due to gunshot wound or fracture of the spinal column since the patients observed were nearly all veterans of World War II. The manifestations of paraplegia, i.e., spastic or flaccid paralysis of the lower extremities, anesthesia generally waist high, paralysis of the bladder and rectum, and intractable bed sores, are so devastating that changes in and about the joints of the lower extremities are usually overlooked or ignored.

Historically, joint changes due to spinal cord injury were mentioned by Charcot in 1868 as a part of his original description of the neuropathic joint which bears his name. The neuroarthropathy of Charcot is also etiologically related to a variety of other neurological diseases, such as tabes, syringomyelia, diseases of the spinal column and cord, trauma to the posterior roots, spina bifida, peripheral nerve injuries, and hemiplegic states. The term "Charcot's joint" includes a variety of joint manifestations, some of which are as dissimilar grossly as their variable etiology. In a general way, this arthropathy is divided into two major groups, the hypertrophic and the atrophic forms. The former is characterized by erosion and fragmentation of the articular extremities and intraarticular and periarticular ossification. In some cases the intraarticular changes predominate, and in others the periarticular changes do. The latter are believed to result from the abnormal stresses and strains placed on the periarticular muscular and connective tissue structures by the unstable fragmented joint.[11] The atrophic Charcot joint differs vastly in appearance from the hypertrophic form. Instead of massive enlargement and fragmentation of the articular extremities and periarticular ossification, one finds in this arthropathy, which is seen especially in the shoulder and hip, erosive enlargement of the socket part of the joint, erosive absorption of the articular extremity of the humerus or femur, as the case may be, and relaxation of the capsule and ligaments, producing the typical "drumstick" appearance. Periarticular ossification is also minimal in this form of arthropathy.

The most common causes of Charcot's joint are tabes dorsalis, in which joint changes occur in from 4 to 10 per cent of cases, and syringomyelia, in which joint changes usually occur in about 25 per cent of cases.[11] In tabes both the atrophic and hypertrophic forms occur, whereas in syringomyelia the atrophic form is most common.

The variable joint changes which are grouped under the term "Charcot's joint" are considered to have the one common feature of occurring in patients with neurological disease. There has, however, been considerable dispute as to the underlying

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† The recent article by Heilbrun and Kuhn: Erosive bone lesions and soft tissue ossifications associated with spinal cord injuries (paraplegia), *Radiology*, 1947, *48*, 579, was published after our paper was completed. These authors stress erosive bone changes in the greater trochanters. This was seen in one of our cases, but was considered to be a part of the erosive process associated with the development of an atrophic Charcot joint. These erosions of the greater trochanters undoubtedly occur more frequently than our small series would indicate, but this does not alter our conclusions as to the nature of paraplegic articular and periarticular changes.

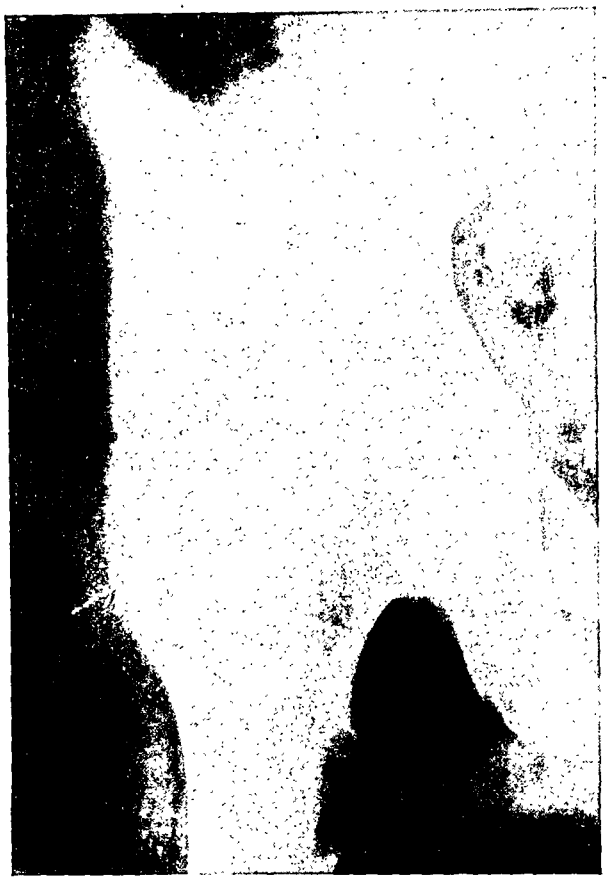


Fig. 1. Case 1. C.E.C., aged twenty-four, gunshot wound of tenth and eleventh dorsal vertebrae on March 23, 1944, with subsequent spastic paraplegia, sensory loss, neurogenic bladder and decubitus ulcers. Roentgenogram taken on June 17, 1946, shows small bony plaque on the outer aspect of the left greater trochanter. Right hip was negative.

mechanism of these joint changes. The mechanical theory advanced by Volkmann attributes the joint destruction to the trauma associated with the continued use of an ataxic joint which lacks certain forms of sensation, or is completely anesthetic. Opposed to this theory is Charcot's original idea that the joint conditions are due to disorder of the normal neurotrophic impulses originating from the central nervous system in these neurological diseases, which impulses are necessary for the normal nutrition of the part. As evidence for the mechanical theory is the experimental work of Eloesser, who demonstrated that trauma in the limb of a cat rendered anesthetic and analgesic experimentally leads to grotesque lesions of the bones and joints which are in every way counterparts of tabetic fractures and arthropathies.[5] It is not proposed to enter into a detailed discussion of the pros and cons of the two theories, but it is sufficient to say that the burden of evidence appears to be in favor of the mechanical theory.

Paraplegia due to disease or injury of the spinal cord has received little notoriety as a cause of neuropathic articular and periarticular changes. Considerable emphasis has been placed in the French and German literature since the first World War on a condition described by the French as a paraosteoarthropathy[1] and by the Germans as a neurogenic myositis ossificans,[6,7] occur-



Fig. 2. Case 11. M. W., aged twenty-eight, fracture of the fifth cervical vertebra in August, 1943, with development of partial paralysis of arms, spastic paralysis of legs, neurogenic bladder, and decubitus ulcers. Roentgenogram taken on June 24, 1946, shows beginning ossification adjacent to the outer aspect of right greater trochanter. Left hip was negative.

ring about the hips and knees of paraplegics. These periarticular ossifications were classified with myositis ossificans rather than with the Charcot arthropathy, although it was recognized that the typical Charcot joint with both intra- and periarticular changes occasionally was seen in the paraplegic and that gradations between the two conditions occurred.

Many theories as to the etiology of this periarticular ossification were offered. It was recognized that fundamentally the condition was related in some way to the lesion in the spinal cord. Some believed that irritative neural impulses set up by the spinal cord were responsible for the soft tissue ossification.[6] Others believed that physical and chemical changes occurred in the paralyzed muscles as a result of edema of the lower extremities,[8] atrophy and degeneration of the muscle fibers,[3] microscopic hemorrhages into the paralyzed muscles, etc.,[3] which resulted in muscle ossification. Inflammatory changes in the muscles[8] possibly related to the deep bed sores were considered, but it has been shown that the ossifications have no anatomical relationship to the decubitus ulcers.[1] The likelihood of an individual diathesis to soft tissue ossification as originally advanced by Virchow to explain myositis ossificans was also brought up, and there is no doubt that some such concept in our present state of ignorance must be used to explain why only about 50 per cent of the cases show these changes. Metastatic calcification secondary to the osteoporosis of recumbency[6] has also been mentioned. However, many of these cases are not recumbent for more than several months, and the condition is actual ossification rather than calcification.

In addition to periarticular ossification in the soft tissues, occasional instances of variable destructive changes in the joints generally associated with the above have also been reported. These have been considered to be typical Charcot's joints,[1,2,7,12] some with hypertrophic manifestations predominant and others with atrophic changes.



FIG. 3. Case III. C. E. B., aged twenty-four, gunshot wound, fourth dorsal vertebra, on January 10, 1944, and immediate spastic paraplegia. Had bed sores over sacrum, greater trochanters, anterior and inner aspects of knees and legs and over both heels. Only in recent months has he developed very slight swelling of the left thigh. Roentgenogram taken on August 13, 1946, shows slight new bone formation above the right greater trochanter. Left hip was negative.

One of our own cases showed periarticular new bone formation about a hip joint initially; but after a number of months, absorption of the head of the femur occurred and also enlargement of the acetabulum producing a classical atrophic Charcot's joint.

Not only may there be a more or less gradual transition between the neuropathic periarthropathy and the arthropathy of the paraplegic, but also between the hypertrophic and atrophic arthropathy of the tabetic. In the latter disease, a joint may initially assume the characteristics of a hypertrophic neuroarthropathy and later those of an atrophic joint.[11]



Fig. 4. Case iv. *A*, right hip; *B*, left hip. J. J. P., aged twenty-five, sustained a fracture of the lower cervical region on May 30, 1940, with immediate paralysis of both lower extremities and arms and loss of function of bowels and bladder. He had swelling of both entire lower extremities, much more marked below the knees, which began about three months after the injury and lasted one month. He had bed sores over the sacrum, left hip, on each heel, and over the left anterior superior iliac spine. Roentgenograms of both hips on June 19, 1946, were negative, but on May 16, 1947, they showed new bone on the outer aspect of both greater trochanters, more marked on the right side and at the attachments to the right lesser and greater trochanters.

Even though these various types of neuroarthropathy may appear to merge with each other and to have certain characteristics in common, the cause of the multiplicity of forms even when produced by a single neurological disease such as tabes has never been adequately clarified. Nor is it entirely clear why the changes in paraplegia are generally confined to periarticular soft tissue ossification, mostly about the hips. However, in the early stages of many of these paraplegic joints, ossification may be seen to begin on the lateral aspect of the greater trochanters, and this suggests that long-continued pressure over anesthetic bony prominences and lack of warning sensation are equivalent to trauma and initiate ossification in the periarticular tissues. The scarcity of intraarticular changes in the paraplegic may be attributed to lack of much use of the insensitive joint due to the additional factor of muscular paralysis,



Fig. 5. Case v. *A*, right hip; *B*, left hip. R. I. J., aged thirty-two, gunshot wound of the third dorsal vertebra in March, 1944. He had a spastic paraplegia and multiple bed sores. Roentgenograms taken on June 19, 1946, showed ossification in the soft tissues about both hips.

so that trauma to the intraarticular structures due to unphysiologic movement does not frequently occur.

In the literature, the soft tissue ossification in paraplegics, other neuroarthropathies, and traumatic myositis ossificans is considered to arise by metaplasia of existing muscular and connective tissue structures, and also by means of traumatic avulsion of shreds of periosteum.[1,6,9] The ossifications in paraplegia are located about the hip joints, attaching to the pelvis and trochanters of the femurs, and also in the muscles on the inner aspects of the thighs extending upwards from the medial femoral condyles. In some cases ossifications about the ankle joints also occur.

In our small series, consisting of 9 cases

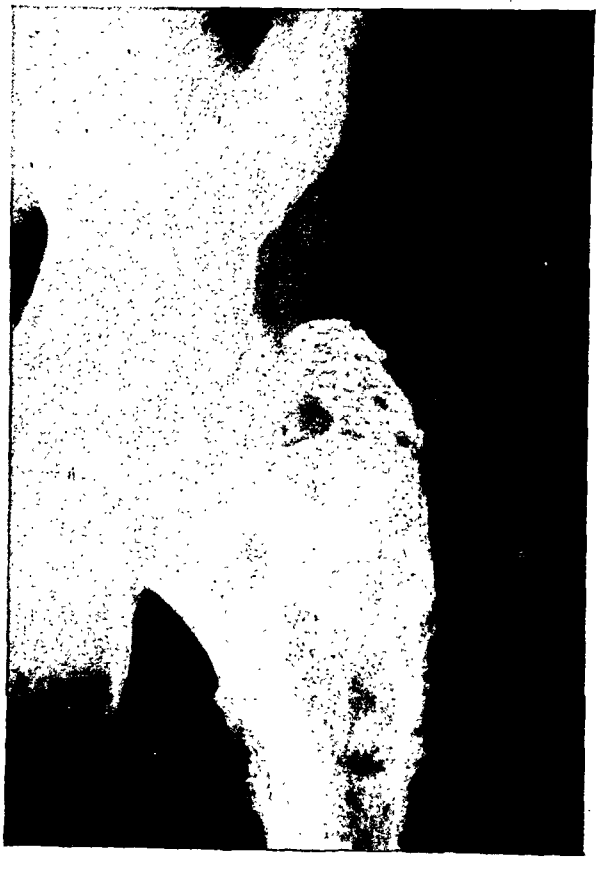


Fig. 6. Case vi. D. T. T., aged twenty-six, sustained a gunshot wound of the lower dorsal region in 1944. He had a flaccid paralysis, anesthesia, and multiple deep infected bed sores. Roentgenograms on November 21, 1945, showed lace-like ossifications attaching to both greater trochanters extending toward the pelvis.

with complete paralysis and anesthesia of both lower extremities, the hip joint regions only were affected. The changes consisted of small bony plaques adjacent to or contiguous with the greater trochanters, often bilateral and symmetrical. In several cases the bony outgrowths extended up toward the pelvis or into the muscles of the thighs. Only one case showed erosion of the articular surfaces characteristic of an atrophic Charcot's joint. All the patients showed slight osteoporosis, but only 2 showed severe osteoporosis of the pelvis and hips, one with periarticular ossification, and the other without it, but manifesting bladder calculi. Of the 9 cases, 7 showed some degree of periarticular ossification. It is felt that this percentage is unusually high and entirely fortuitous in that the figure of slightly less than 50 per cent given in the literature[1,3] probably more closely approximates the true state of facts. Of the 9 cases, 7 had a spastic paralysis and 2 a flaccid paralysis. Five cases were due to gunshot wound of the dorsal spine, 3 to fracture of the spinal column, and one to a meningioma in the dorsal region. Almost all the cases had bed sores of greater or lesser severity, but edema of the lower extremities was not a conspicuous feature of any of the cases at any time.



FIG. 7. Case VII. D. D., aged twenty-six; fracture dislocation of the twelfth dorsal vertebra on November 19, 1945, with flaccid paralysis and anesthesia. Left leg had to be amputated at mid-thigh level. His right foot swelled slightly for about a month after the injury but not since then. He had bed sores over the sacrum, greater trochanters, iliac crests, head of right fibula, right heel and outer aspect of right foot and lower leg. Roentgenograms taken on June 24, 1946 (*A*, right hip), showed ossification in the soft tissues about both hips. On April 10, 1947, the left hip was unchanged, but the right hip (*B*) had developed into a typical atrophic Charcot's joint with erosion of the head of the femur, acetabulum and trochanters. There was considerable osteoporosis.

Teleologically speaking, the periarticular ossification might be considered to serve as an internal splint for the paralyzed joints

in the same way that Steindler has postulated that the ossification about an unstable tabetic joint may act as a splint.[11] Unfortunately, the ossification is rarely complete enough in the paraplegic to serve as such, although circumferential ankylosis of a hip joint has been described.[1] In addition, the joint may be fixed in an unfavorable position. It is therefore concluded that in the paraplegic, the ossifications and joint changes, when they occur, are not in in any sense purposive or desirable but merely neuropathic changes in an anesthetic paralyzed member, related to the neuroarthropathies of other neurological diseases.

SUMMARY

Neuropathic articular and periarticular changes occur in the lower extremities of paraplegics, constituting another example of the Charcot neuroarthropathy. In Charcot's joint, there may be intraarticular destructive and productive changes and also extraarticular soft tissue ossification—the hypertrophic variety; or there may be erosion and absorption of the articular extremities with relaxation of the capsule and ligaments—the atrophic variety. Periarticular ossification may be massive or minimal in either type. In the parapelgic, periarticular ossification is the outstanding feature, and intraarticular destructive changes are minimal or absent, though occasionally striking. Transitions between the various forms of neuroarthropathy may occasionally be seen.

The mechanism of the paraplegic neuroarthropathy is believed to be long-continued pressure over anesthetic bony prominences and lack of warning sensation, which are equivalent to trauma in initiating ossification in the periarticular tissues. The scarcity of intraarticular changes is attributed to lack of use of the paralyzed joints.

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DOUBLE CONTOUR, CUPPING AND SPURRING IN ROENTGENOGRAMS OF LONG BONES IN INFANTS*

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VERY little has been written on roentgen diagnosis in children in this country, and Caffey mentions in his book, "Pediatric X-Ray Diagnosis"[1a]: " . . . As far as I have been able to determine no book on pediatric roentgen diagnosis has been published in English during the 35 years which have passed since Rotch's unique publication in 1910."[2] Indeed a search through the literature in this country and abroad produced very few publications referring to normal roentgenograms in children, especially of the bones.

The purpose of this paper is to describe findings consisting of a "double contour," "cupping" and "spurring" seen on routine roentgenograms of the long bones, findings which have certainly been observed by roentgenologists and pediatricians who have the opportunity of seeing large numbers of roentgenograms of normal babies. These findings, to my knowledge, have not been discussed thoroughly in the literature and frequently lead to misinterpretation.

The only reference to these roentgen findings in the medical literature was found in Caffey's book: " . . . the ulna and occasionally the radius may form a curved (cupped) transverse surface instead of the usual straight plane at right angles to the long axis of the shaft. This physiologic cupping has been described in many nonrachitic infants. . . . "[1b] " . . . The interosseous ridge on the medial side of the shaft may cause an extra shadow which simulates asymmetrical subperiosteal cortical thickening . . . "[1c] " . . . On the superior aspect of the lateral margin of the tibial shaft, the ridge for the insertion of the tibialis anticus muscle should not be misconstructed as a regional thickening of the cortex."[1d]

Unfortunately, however, the book fails to show illustrations of these findings, nor does it give a numerical interpretation of the frequency and time of occurrence or a pathologic investigation as to the reason for the appearance of these pseudo-pathologic findings.

McLean and McIntosh[3] in 1928 made the following statement: " . . . Another source of difficulty in the interpretation of spurs arises from the fact that the zone of preparatory calcification actually presents in the x-ray the projected shadow of a disk. . . . "

These were the only references which could be found, and even complete works such as Wimberger's[4] clinical-roentgenological diagnosis of rickets, scurvy and syphilis, Rotch's[2] book or Köhler's Röntgenology[5] do not mention these observations.

The tables of our study bring a report of 100 consecutive prematurely born babies observed at a Premature Follow-up Clinic at Cook County Children's Hospital during the years 1945–1947. Roentgenograms of the long bones, wrists and ankles were taken routinely at monthly intervals up to their eighth month of life. Thus the total number of roentgenograms viewed is approximately 800. The growth and development of these babies were apparently normal.

In viewing these roentgenograms we have noticed several findings on long bones of these infants which were in the beginning frequently interpreted by us and by others as signs of rickets, scurvy or congenital

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syphilis. The large number of roentgenograms taken, however, and the close supervision and study of these babies led us to the conclusion that these findings were physiologic and that their interpretation as signs of pathology was incorrect. This was later proved by the fact that the forearms of the child were placed flat on the film in pronation, thus getting a postero-anterior view of the forearms and hands, parallel position of the ulna and radius and good visualization of the distal epiphysis. The lower extremities were placed in a lateral position on the film in order to pro-

TABLE I

MONTH OF FIRST VISIBILITY OF "DOUBLE CONTOUR" (100 INFANTS)

Bone	1st	2nd	3rd	4th	5th	6th	7th	8th	Total
Ulna	*	*****	********	********	********	********	**	***	78
		****	*******	********	***	********			
				***		**			
	1	9	15	19	11	18	2	3	
Radius	*	***	********	********	********	********	*****	****	76
			*******	********	**	*******			

	1	3	15	23	10	15	5	4	
Tibia	*	****	********	********	******	******	*		49
			********	****					

	1	4	19	12	6	6	1		
Fibula			*****	********	****	*****	*****	*	28
			5	8	4	5	5	1	

MONTH OF FIRST VISIBILITY OF "CUPPING" AND/OR "SPURRING" (100 INFANTS)

Ulna		***	********	********	********	********	*	***	73
			********	********	*****				
			********	****					
		3	* 25	20	13	8	1	3	
Radius			********	********	********	****	*	***	46
				********	****				
			8	** 18	12	4	1	3	
Tibia			** 2	*** 3	* 1	*** 3			9
Fibula			* 1	*** 3		** 2			6

Note: Each asterisk indicates a case which showed the "double contour," "cupping," or "spurring" for the first time during the respective month.

"double contour" as well as the "cupping" and "spurring" disappeared spontaneously without any change in management.

The technique of taking the roentgenograms was the routine method of "long bones, wrists and ankles" films. Hands and duce a view of the distal epiphysis of tibia and fibula. A true anteroposterior view would distort the picture of the epiphyseal line because of the distance produced by the protruding heel. The lateral view, unfortunately, does not permit a complete



Fig. 1. "Double contour" on ulna and radius in a five month old healthy prematurely born infant.

visualization of the fibula and tibia, as some parts of these bones are always overshadowing each other in this position.

The observations can be described in short as follows: The surfaces of the long bones of the forearm and shank were frequently outlined by a double contour which gave the impression of periosteal thickening or elevation and/or cortical hypertrophy. These lines may be present on all four bones of the distal parts of the extremities or on only one or more; they were seen most frequently on the ulna, and with decreasing frequency on radius, tibia and fibula (see Table 1). Frequently they appeared on one bone first and became visible on some of the other bones as well on roentgenograms taken one or more months thereafter. These lines may cover the entire length of the bone, from metaphysis to metaphysis, or may be very short, beginning at one end of the bone, emerging from the periosteum, paralleling it in about 0.5 to 1.0 millimeter distance and fading into the subcortical structures. The line itself is usually smooth, but occasionally shows thickening or thinning of its shadow (Fig. 1 and 2). In the largest number of cases this double contour was observed for the first time during the third or fourth month of life. In following up these findings we noted that the lines began to be less frequently visible around the seventh and especially the eighth month of life (Table II).

A second observation was the peculiar appearance of the epiphyseal line, showing some characteristics which at times may be interpreted as signs of disease. The orthodox picture of the epiphyseal plate is a straight line. However, if the roentgen rays traverse the epiphyseal plate at an angle other than a right one, it may appear concave or convex and the edges will then



Fig. 2. "Double contour" on tibia and fibula in a seven month old healthy prematurely born infant.

seem elongated, which resembles the "spurring," "lipping," or "cupping" as seen in scurvy and rickets. At times bizarre pictures of waves or ellipses may be seen (Fig. 3 and 4). This "cupping" and "spurring" became first visible in most cases around the third and fourth month of life and began to disappear in many cases around the seventh and eighth month (Tables I and II). The reason for this disappearance in later life is probably the fact that the more intense calcification of the bone does not permit penetration of the rays in these older babies and thus prevents the visualization of a second shadow. This will be further elaborated later.

It should be noted that these above mentioned figures (Tables I and II), although probably true enough to give a good account of the frequency at which these phenomena can be observed and therefore of the chances for misinterpretation, may not be accurate if taken from a purely statistical point of view. To explain this fact, some of the shortcomings in the technique may be mentioned here. If the lower

TABLE II

MONTH OF DISAPPEARANCE OF "DOUBLE CONTOUR" (100 INFANTS)

Bone:	1st	2nd	3rd	4th	5th	6th	7th	8th	Total
Ulna			* 1		** 2	*** 3	****** 6	******** ******** **** 20	32
Radius			* 1			****** 6	**** 4	******** ******** 16	27
Tibia				* 1		****** 6	**** 4	******** ***** 13	24
Fibula						** 2	* 1	***** 5	8

MONTH OF DISAPPEARANCE OF "CUPPING" AND/OR "SPURRING" (100 INFANTS)

Ulna					* 1	**** 4	******** ******** 16	******** ******** ******** ****** 30	51
Radius				* 1	* 1	**** 4	******* 7	******** ******** *** 19	32
Tibia						** 2	* 1	****** 6	9
Fibula								***** 5	5

Note: Each asterisk indicates a case which for the first time during the respective month *failed to show* the previously visible "double contour," "cupping" or "spurring."

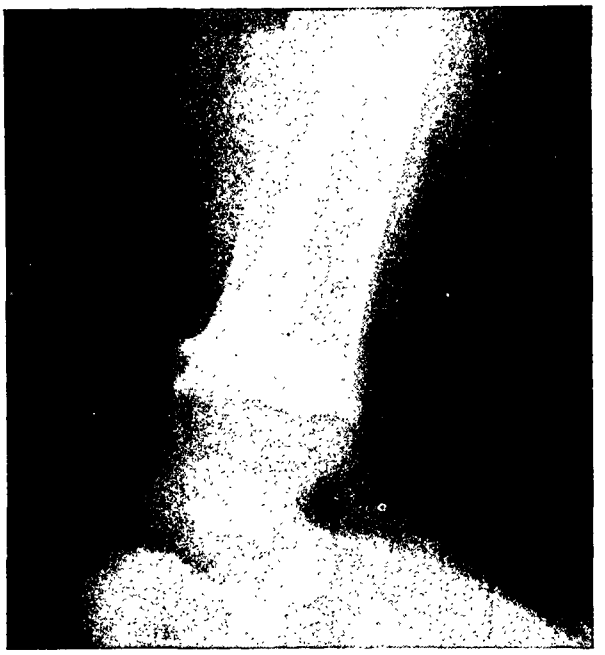


Fig. 3. "Wavy" epiphyseal line of tibia and fibula in a five month old healthy prematurely born baby.

legs are viewed in a true anteroposterior position, the heel of the foot, especially in Negro children, will prevent the parallel apposition of the fibula and tibia to the film. The result is a distorted, not sharply outlined view of the distal epiphysis, which does not permit the interpretation of the epiphyseal line. On the other hand, if we take a lateral view of the lower leg, which in general was done, the epiphyseal lines were well outlined and visible, but the shadow of the tibia and fibula were partially or totally overlying, thus prohibiting a true interpretation of the periosteum and the "double contour." We were unable to fully overcome this difficulty, but did not find any special need for doing so. In the individual case two roentgenograms, one in true anteroposterior and one lateral, or one well placed oblique view, would answer the problem. We may also add at this point that due to technical difficulties, such as

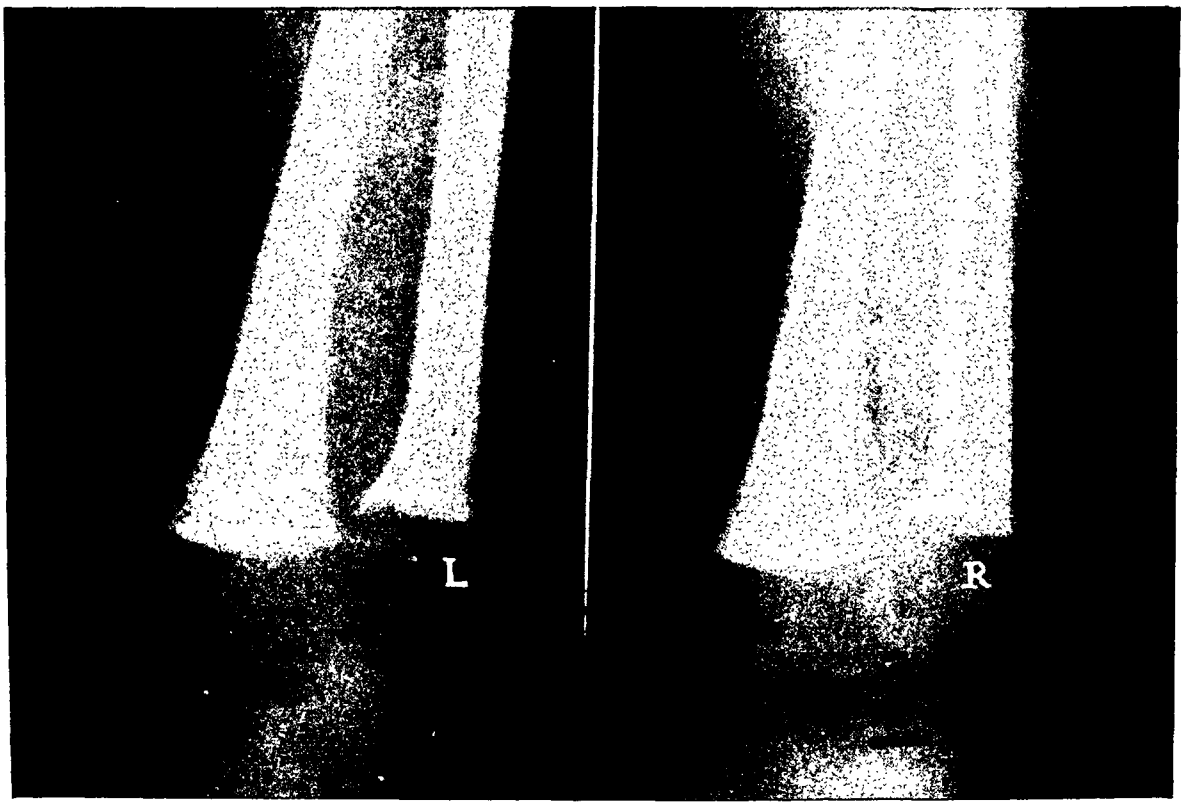


Fig. 4. "Cupping" and "spurring" seen in the roentgenogram of right ulna but almost unnoticeable on the roentgenogram of the left ulna of a three month old baby, taken at the same time but with slightly different angle.

movement of the patient during exposure, and so forth, certain views were missing, which may further alter the exact numerical relationship of appearance, disappearance and incidence. We do not believe, however, that any of the above mentioned shortcomings would alter the sense or interpretation of this paper materially.

In order to compare the findings on our premature infants with findings on full term babies, an unselected group of 100 patients, admitted to the Hospital for various reasons obviously unrelated to the growth or development of the bones, was chosen and the same type of roentgenograms as of the premature group were taken. The infants' ages ranged from one to eight months. One roentgenogram was taken of each infant. Of 67 babies who fell into the age group from two to six months, double contour was seen on the ulna in 46, on the radius in 37, on the tibia in 24 and on the fibula in 14 roentgenograms. The incidence of the visibility of these lines during the first, seventh and eighth months was considerably lower. Spurring and cupping was found most frequently between the third and fifth months. The total incidence of spurring and cupping was lower in this group than in the premature babies. This sample group of average newborn to eight month old infants demonstrates that the "double contour," "cupping" and "spurring" are not a characteristic of the premature baby, but occur in the full term child as well.

Although statistically the group of full term infants is not comparable with the group of premature babies, because only one roentgenogram was taken of each of the full term babies and thus the "first appearance" was not determined but only the general incidence, the figures show that the "double contour" tends to occur earlier (second month) and to disappear earlier (fifth month) in the full term babies, as would be expected because of their higher degree of maturity and greater density of calcification of their bones.

The occurrence of a "double contour," "cupping" and "spurring" was also studied on a smaller number of roentgenograms of femur (56) and humerus (42) of the same groups of premature children. The double contour was found to be less frequent in this group (femur 17, humerus 15). This lower incidence corresponds to the rounder form of the transverse section of these bones which will not so readily permit the appearance of a double shadow. The cases in which double lines were seen were due either to the increased prominence of the posterior crests, to clearer separation of cortex from marrow, or to a clearly visible canal of the nutrient artery. The absence of "cupping" of the distal epiphysis of the humerus and femur is easily explained by the convexly curved character of the epiphyseal plate.

The small number of roentgenograms of full term babies prohibits numerical evaluation of the incidence of these phenomena in this group, but suffices to prove their existence.

Extensive examinations of the blood, chemically, for calcium, phosphorus, phosphatase, and serologically, of the babies used for this study, did not reveal any signs of pathology. The graphic and statistical evaluation of the growth and development of these babies proved their normal progress as compared with standard figures. A histopathological examination of the cross-sections of all four bones (radius, ulna, tibia, fibula) of one of the babies who showed the above described double lines and died of interstitial pneumonitis also revealed normal structure as shown by the pathologist's report: "The microscopical examination of the sections taken from the tibia, fibula, radius and ulna showed normal spongiosa and compacta. The periosteum was of appropriate thickness and structure, no inflammatory reaction (exudation, congestion of vessels, proliferation of connective tissue) was observed. The architecture of the bony structures was normal, the bone marrow showed myelo-erythropoietic activities."

The explanation of these double lines

can be made by a careful observation of the anatomical structure of the bones, especially their crests and the direction of the roentgen rays in relationship to the bone and the film (Fig. 5).

The more intense shadow of the cortex of the shaft will produce occasionally a line parallel to the outer contour of the bone and visible mainly in the middle third of the shaft. On certain films the canal of the nutrient artery of the bone can also produce a similar effect. This last phenomenon, however, does not give rise to misinterpretation by the experienced. The much less frequent visualization of the double line in the tibia (49 per cent) and the fibula (28 per cent) as stated in our table, may not only be attributed to the different shape of the cross-sections of these bones but also to the technical difficulty of good visualization of the entire outline of both bones as described above.

The explanation of "cupping" and "spurring" may also be found in the projection of the anatomical form of the epiphyseal plate (Fig. 6).

For further study and better demonstration the radius, ulna, tibia and fibula of a four and a half month old, prematurely born infant who died of a condition unrelated to bone growth, were removed at necropsy, freed of most adherent soft tis-

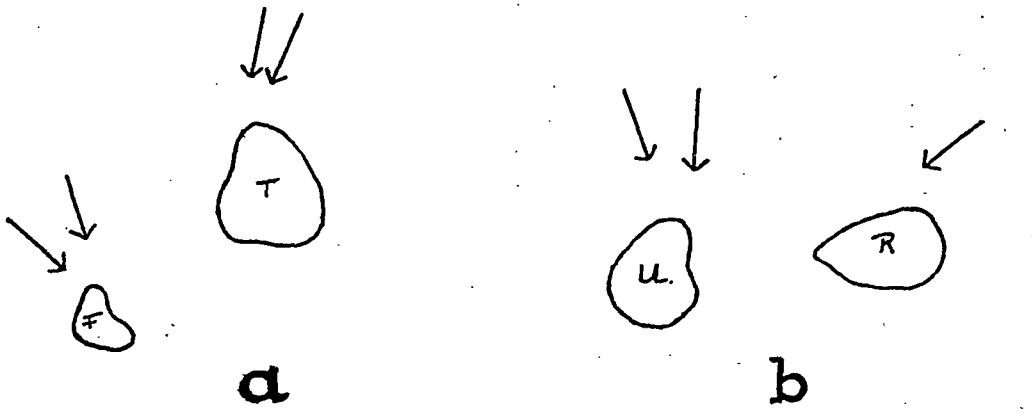


Fig. 5. Drawing of cross-section through (*a*) fibula and tibia and (*b*) ulna and radius, indicating the arrangements of crests running along the anterior, lateral and medial aspects of the bone which may, under a certain relationship of the position of tube, bone and film, as indicated by the arrows, produce a double line.

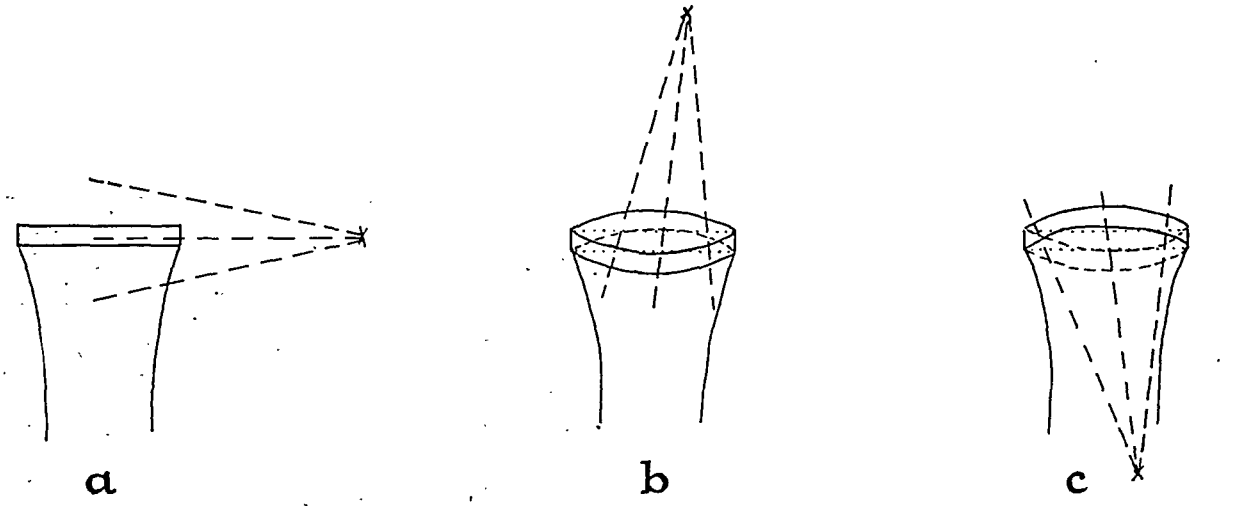


Fig. 6. (*a*) Rays hitting parallel to the epiphyseal plate produce a straight line; (*b*) and (*c*) Rays hitting at acute angle will produce an appearance of cupping or bulging depending upon degree and direction of opening of angle.

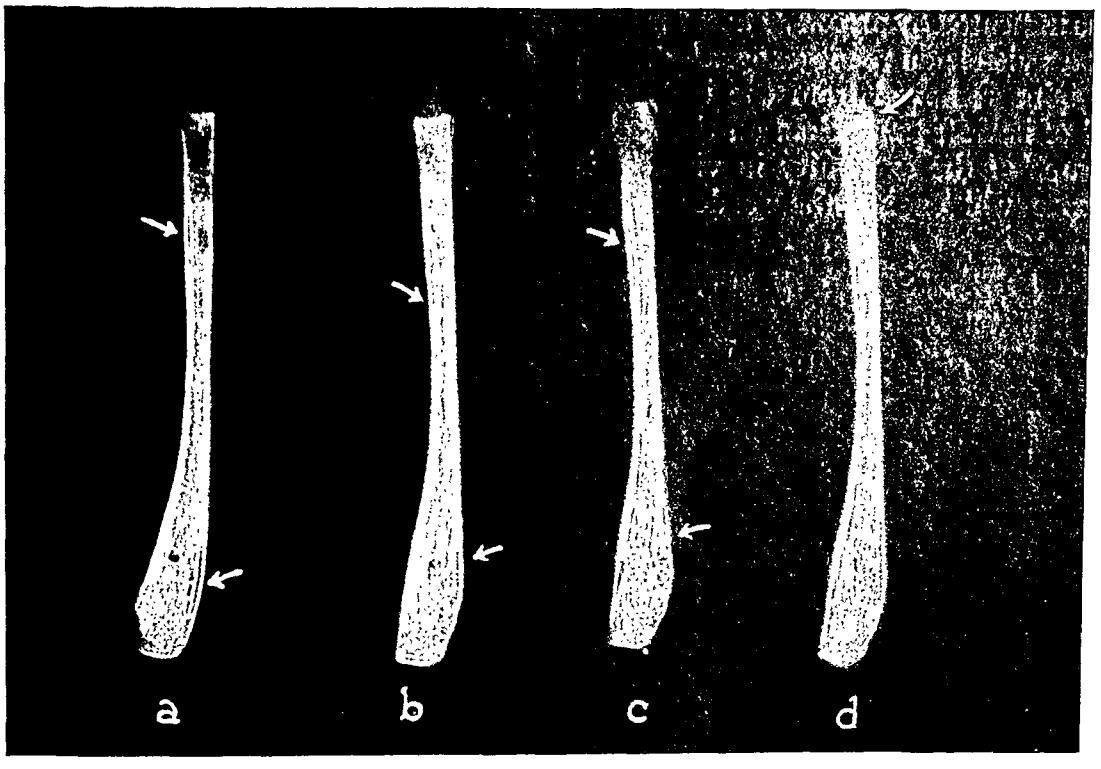


Fig. 7. *Right ulna* (*a*) turned 15 degrees to the left of the true anteroposterior position: double line visible on lateral aspect of proximal third and medial aspect of middle third of bone; (*b*) true anteroposterior position: same double lines visible but less pronounced; (*c*) inclined 15 degrees to the right: double line on proximal third has practically disappeared; line in the middle third is better visible than in (*a*) and (*b*); (*d*) anteroposterior position with the roentgen tube placed distal to the bone and focused on the bone at an angle of 20 degrees: epiphyseal plate projects in form of a curved line (cupping) whereas (*a*), (*b*) and (*c*) show it projected essentially as straight line.

(The dark spot in center of proximal third of bone is an artefact and was produced by a drill perforation in an attempt to find a method for stabilization of the bone and exact measurement of the angle. The final technique used was the fixation of a wooden stick to the bone and a vertical wire attached to the stick as pointer. This permitted accurate measuring of wire's and thus bone's angle in relation to the tube.)

sues, and studied roentgenographically and histologically.

The following roentgenograms (Fig. 7, 8, 9 and 10) demonstrate the visible "double line" and also the "cupping" and "spur-

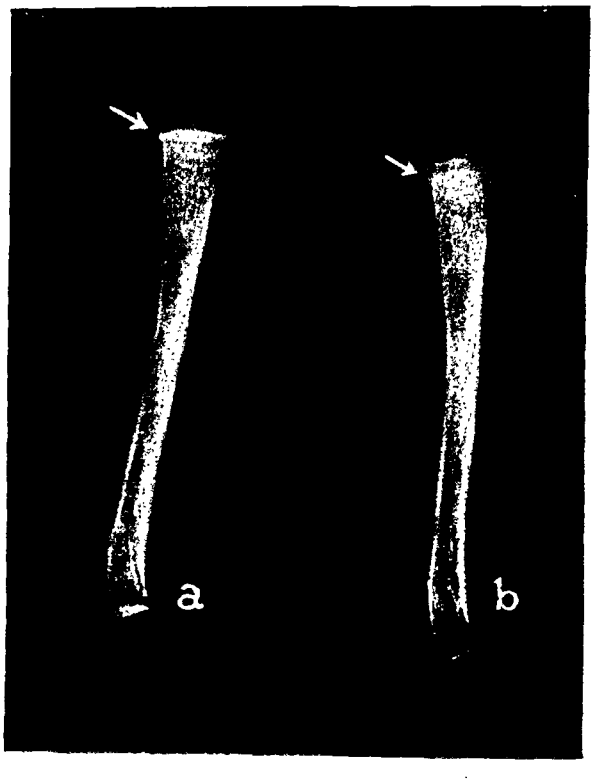


Fig. 8. *Right radius:* (*a*) in anteroposterior position with tube directly above bone: epiphyseal plate projects at straight line; (*b*) in anteroposterior position, with roentgen tube placed distal to the bone and focused on the bone at an angle of 20 degrees: epiphyseal plate now projects as curved line.

(The soft tissue shadow distal to the radial epiphysis was produced by the incompletely removed joint capsule.)

ring" as indicated by arrows. These findings are better visible on roentgenograms taken of the bone removed from the body and cleared of its soft parts than on the roentgenograms of the extremity in vivo. This experience will enable the reader to acquaint himself with the described lines and to recognize them more readily on the ordinary roentgenogram. To show that and how these lines vary if the angle between rays and bone is changed, a series of roentgenograms was taken at different positions. It is evident from these roentgenograms that the intensity, position or length of the double contour or the appearance of the projection of the epiphyseal plate varies with the position of the roentgen tube. This explains the fact that only a certain number of "routine roentgenograms" will actually show these phenomena and that changes in the position of patient and tube, which to a minor degree occur constantly on "routine roentgenograms," will be responsible for the more or less frequent appearance and the variation in different bones of children of the same age group.

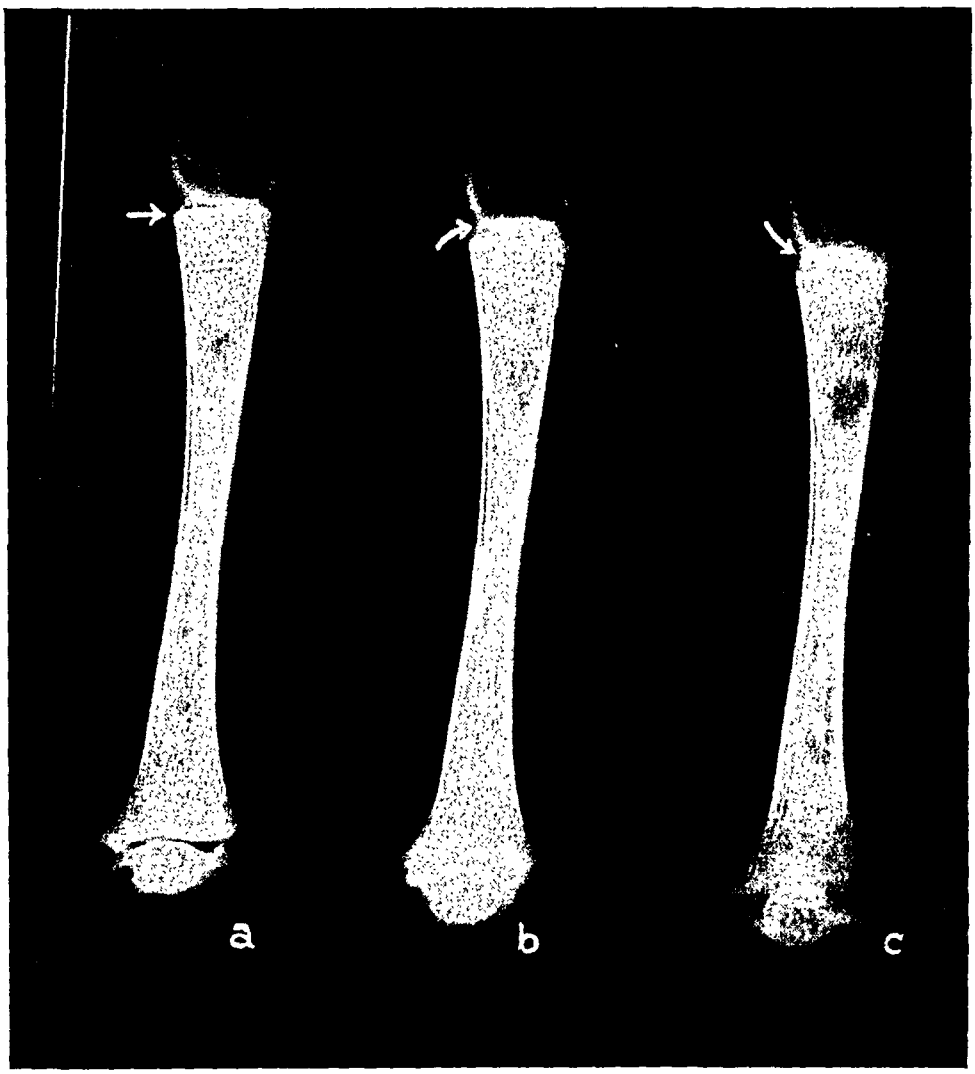


Fig. 9. *Right tibia*: anteroposterior position with the tube (*a*) accurately above the bone (straight epiphyseal line projection); (*b*) distal to the bone, focused on the bone at an angle of 25 degrees (convex epiphyseal line projection); (*c*) proximal to the bone, focused on the bone at an angle of 25 degrees (concave epiphyseal line projection).

The data in Tables I and II were arrived at by the study of a large number of roentgenograms taken at various times by different technicians, and indicate only the incidence of the visibility of the above phenomena in the roentgenograms and mit the visualization of the above described phenomena at this time. Progressive calcification of the entire bone in the subsequent period decreases the visibility of finer details and thus causes the disappearance of the findings. The period from three to

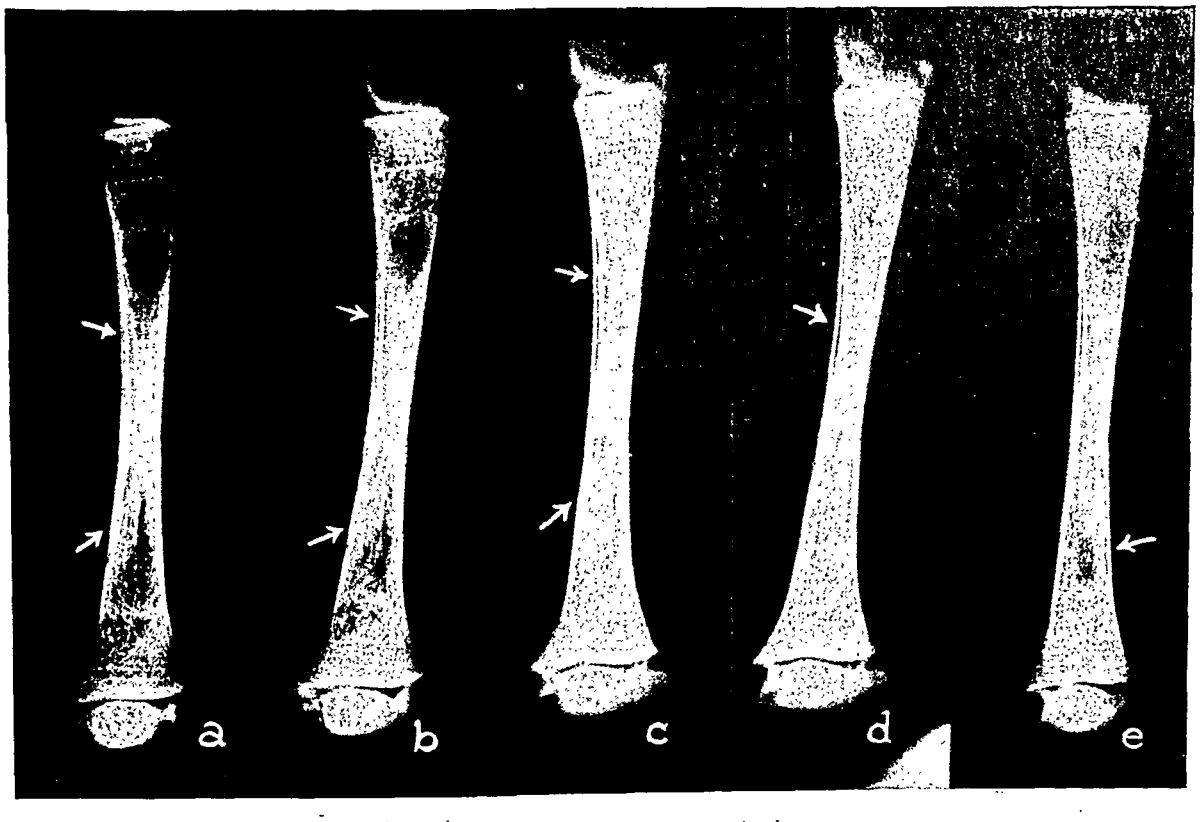


FIG. 10. *Right tibia* (*a*) turned 25 degrees to the right of the true anteroposterior position, showing double line on medial aspect of middle third and on proximal third; (*b*) turned only 15 degrees in the same direction makes line in middle third better visible but reduces visibility of line in proximal third; (*c*) true anteroposterior position: line in middle third well visible, in proximal third line has almost disappeared; (*d*) turned 15 degrees to the left: line on middle third well visible but progressively shorter; proximal line no longer visible; (*e*) turned 25 degrees to the left: a new "double line" appears on lateral aspect of proximal end.

not the absence or presence of an anatomical structure. The two tables demonstrate very well, however, the relative frequency of occurrence during certain months of the child's life. The explanation for this temporary visibility may well be the poor calcification of the entire bone which prohibits visualization of the crests during the first weeks of life; the increased formation and calcification of prominences during the following months and the still relatively roentgen transparent bone per-

six months of life in our premature infants and roughly from two to five months in full term babies corresponds to this interim period during which "double contours," "cupping" and "spurring" can be seen with greatest frequency, and it is also this age period during which the differential diagnosis of congenital syphilis, scurvy and rickets has to be taken into special consideration.

Microsections, prepared from the same bones after the above roentgenograms were

taken, demonstrate the normal structure of the bone as seen from the report of the pathologist: *Transverse section*—cortex and spongiosa show normal architecture. Periosteum is of normal thickness. *Diagonal section*—at the epiphyseal line the cartilage shows the typical arrangement into resting, proliferating and columnar zone of cartilage cells. The bone trabeculae are of normal width. The primary bone marrow cavity is filled with normal bone marrow. The *section* in the *frontal plane* shows the typical picture of endochondral ossification. In the hyaline cartilage the cartilage cells are arranged in columns in a typical fashion. The zone of proliferating cartilage cells is of normal width. Nearer the zone of ossification the flat cartilage cells are swollen. The metaphysis is composed of spongy bone substance consisting of trabeculae of normal width, arrangement, and mineral content. The bone corpuscles show the orderly arrangement of bone corpuscles in normal ossified tissue. *Summary:* The sections taken in various directions reveal the regular sequence of events characterized by proliferation of cartilage cells and conversion of the osteoid tissue into regular bone.

SUMMARY

Monthly roentgenograms of 100 healthy, prematurely born infants from birth to eight months were viewed and studied. A double line in the contour of the long bones of the extremities and a cupped and spurred appearance of the epiphyseal line of the same bones were observed frequently. These phenomena may be misinterpreted as signs of a pathological process. However, we have tried to demonstrate that these findings do occur in healthy premature and full term infants, that histopathologic examination of sections through the bones of infants who showed these lines in vivo and died of unrelated conditions are also normal, that they are most frequently seen in the age group from two to six months and that their later disappearance occurs without any treatment or change in management, and that the findings can therefore be considered as a normal roentgen appearance of the long bones during the process of growth.

I wish to express my appreciation to Dr. John Caffey, Babies Hospital, New York, for his valuable suggestions which helped materially in the completion of this paper, and to Dr. P. R. Szanto, Department of Pathology, Cook County Hospital, for procuring and interpreting the pathologic specimens.

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Vol. 61, No. 4

SESAMOID BONES OF THE HANDS AND FEET

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IN 1940 Francis[9] presented Brush Foundation data for the appearance of ossification centers from 6 to 15 years. In the course of that study he observed the sesamoid bones to be more numerous in the females of the fifteen year age group. At Dr. Francis' suggestion this author began an investigation of the sesamoids of the hands and feet to see whether or not a definite sex-limited factor existed. The scope was then broadened to include a general review of the sesamoids of the hands and feet.

From the files of the Brush Foundation, Western Reserve School of Medicine, roentgenograms of 529 hands and 510 feet were reviewed. Young adults who had reached, or nearly reached, maturity, according to the Todd method of assessment of skeletal age were used. Cases were selected at random from the files according to age, excluding only those cases which showed definite endocrine disturbances. All roentgenograms examined were of the left extremity. Table 1 shows the sex distribution of the cases reviewed:

TABLE I

		Hands	Feet
18–30 years	White males	299	286
18–30 years	White females	230	224
TOTALS		529	510

HISTORICAL

The sesamoid bones, resembling grains of Indian wheat, are certain very round small Bones, somewhat flat and spongy within. They adhere at the Joynts to the tendons of the muscles that move the fingers and toes, and with them in the boyling of dead Carkasses, and the purgation and denudation of the bones are utterly lost unless great care be taken to preserve them.

It would be a difficult matter to find in any modern textbook of anatomy an account so full and good of these curious little bones as that given by Diemerbroeck (1609-1674), from whose work this quotation was made by Jones.[15]

The study of sesamoid structures, due to their size and frequent variations, has attracted of late but little attention. The medial sesamoid bone of the big toe has been identified by Garrison[10] as the bone "Luz," a mythical bone believed in medieval times to be the indestructible seed from which the body would be resurrected on the Day of Judgment.

The term "sesamoid" denotes the similarity between the size and shape of the bones, and that of the flat, oval seeds of the *Sesamum indicum*, an ancient East Indian plant used by the Greek physicians for purging. The name is said to have been applied by Galen.

Pfitzner,[22] in 1892, published his classical exhaustive monograph on the sesamoid bones and their variations, from dissection data of many cadavera, including 1,440 hands. The first correlation between the anatomical dissections and roentgenography of these bones was presented by Fawcett[7] in 1896. Of interest is his reaction to the clarity of early roentgenograms:

> Through the kindness of Mr. Chattock, Professor of Physics in University College, who has shown the greatest possible interest in the subject, I have been able to examine the hands of thirty-eight of my own students, and three of his by means of skiagraphy. The results exceeded in every way my fondest hopes. Not only were sesamoid bones clearly portrayed, but the cancellous tissue of the various bones was depicted in a delightfully clear manner.

ANATOMIC CONSIDERATIONS

Thilenius, cited by Lapidus,[19] proved conclusively the presence of cartilaginous anlagen for the two sesamoids beneath

each metacarpal head in a number of human embryos at about the third or fourth month. Inge and Ferguson[14] studied the development of sesamoids of the feet in the human fetus ranging in age from 8 weeks to 9 months. At the eighth week they found that both sesamoid bones are recognizable as islands of undifferentiated connective tissue in their normal location beneath the first metatarsal head. At the tenth week this connective tissue can be recognized as precartilaginous, and at the twelfth week there is a definite center of chondrification. These changes occur simultaneously in sesamoids, phalanges and metatarsals. The connective tissue in which the sesamoids develop is seen to be continuous with the periosteum of the metatarsal proximally, and with that of the phalanx distally; by the third month this can be identified as joint capsule, and the fibers of the tendon invest the lower portion of the bone between the third and fourth months. By the fifth month these bones have their normal adult shape, and the development from then on is in size. At no time did they find any evidence of formation from cartilaginous buds from the phalanx.

In the adult hand, as a rule, there are five sesamoids. Two of these lie at the metacarpophalangeal joint of the thumb in the tendinous insertion of the flexor pollicis brevis and the adductor pollicis. They are blended with the palmar ligament of the joint, and articulate with the palmar surface of the metacarpal bone. One sesamoid may be present at the interphalangeal joint of the thumb and two others at the metacarpophalangeal joints of the index and little fingers respectively. Sometimes not all five are present, and occasionally there are extra sesamoid bones in both the metacarpophalangeal and interphalangeal joints.

Lapidus[19] believes that, in the feet, sesamoids may occur in the lumbrical, and rarely in the interosseus tendons at the joint surfaces over which they act, an observation with which I concur, having noted several cases both in hands and feet which appeared to be in this anatomical location.

In the foot two sesamoid bones are almost constantly present at the metatarsophalangeal joint of the great toe. Each is enclosed by the corresponding tendon of the flexor hallucis brevis and the articular capsule, and articulates with and rests under the metatarsal head of the great toe, the cartilage of the latter being prolonged proximally for that purpose. The sesamoids are separated from each other by the tendon of the flexor hallucis longus. Between the sesamoids and the skin there is, normally, only the thick fibrous pad of the "ball" of the foot, through which the two small bones may occasionally be palpated. Not infrequently a bursa is interposed between the sesamoid and the skin. Other sesamoids occur at the other metatarsophalangeal joints, the interphalangeal joints and, occasionally, in the lumbricals and interossei. These will be discussed in greater detail in a later section.

The sesamoid and supernumerary bones of the carpus, tarsus and limbs are outside the scope of this presentation but Bizarro,[2] Dwight,[6] and Holland,[12] Burman and Lapidus,[5] and others, give excellent accounts of these interesting structures.

Lapidus[19] examined 320 extremities of various mammals in the New York Museum of Natural History; 56 fossils, 192 primates and 72 other mammals with special reference to the sesamoids. Two sesamoids were found beneath each metacarpal or metatarsal head in almost all adult specimens including the 56 extremities of the fossil animals.

It is difficult to give a conclusive reason for the existence of the sesamoid structures in the human body. Bizarro[2] in a remarkably complete study reviewed the comparative anatomophysiology and concluded that both phylogeny and function, combined, appear to be the two causes of sesamoid formation and development. The former originates and plants, as it were, the seeds for their formation, and the latter,

acting daily and with every movement, promotes the increase of size of these structures.

OSSIFICATION CENTERS

Ossification of the sesamoids has been studied extensively at this institution. The late T. Wingate Todd in his Atlas[27] described beginning ossification of the pollex sesamoids at about 12 years 9 months for males, and 11 years 9 months for females.

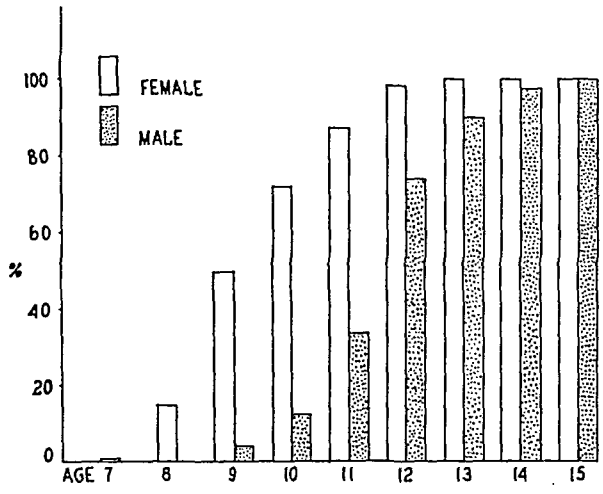


Fig. 1. Comparative time order appearance of ossification centers of the hallux sesamoids; showing percentage of ossification in males and females by years. (Courtesy of C. C. Francis.)

Todd[26] observed that there is a minor progressive acceleration of female skeletal maturation between 6 and 8 years. During the period 8 to 9 years the females slow up so that the male maturation reaches that of the female at about the latter date. At 10 years, the girls again advance ahead of the boys, and shortly after the thirteenth birthday are already at the stage reached in the boys about the fifteenth birthday. Thereafter, they slow down once more and at about 16.5 years the maturation of the male skeleton has finally caught up with the female.

Flory[8] found that 50 per cent of the girls in his series showed beginning ossification of the metacarpophalangeal sesamoid of the thumb at 11 years, and 50 per cent of the boys at 13 years. Francis[9] gives the comparative time order appearance of ossification centers of the pollex and hallux sesamoids as shown in Figures 1 and 2.

Ossification may occur from multiple centers which may, or may not, unite subsequently. Failure of union of these centers is believed to give rise to the partite appearance of these bones in the roentgenogram.

Baldwin[1] reported that sesamoids at the the thumb appear two years earlier in the

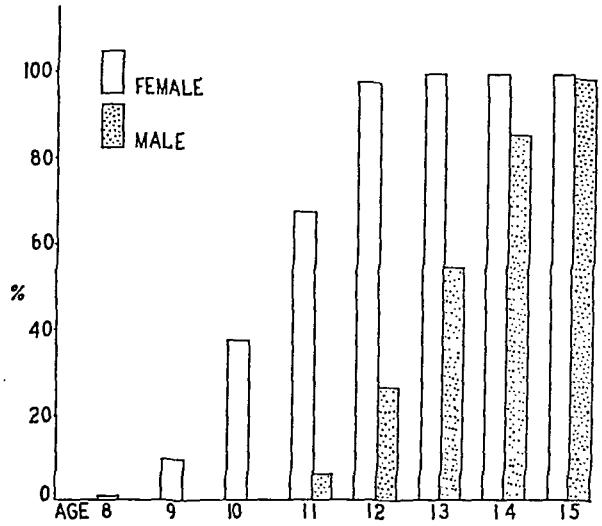


Fig. 2. Comparative time order appearance of ossification centers of the pollex sesamoids; showing percentage of ossification in males and females by years. (Courtesy of C. C. Francis.)

female than in male hands; from 10–14 years for girls and 12–16 years for boys. Flory[8] states that pubertal onset can be predicted fairly well by the appearance of the sesamoid bone at the distal end of the first metacarpal. This sesamoid appears in girls' hands about two years before the first menstruation. Buehl and Pyle[4] working in the Brush Foundation found that in 30 girls the average age of onset of ossification of the pollex sesamoids was 10.1 years; for 30 boys it was 12.6 years. They found that the mean menarche was 12.7 years for the 30 girls, these findings being in agreement with Flory. Rochlin, cited by Flory, concluded that sesamoids always appear before the sex glands begin their secretion in the endocrine system, before

Table II

PERCENTAGE DISTRIBUTION OF SESAMOID BONES IN THE HAND IN MALES AND FEMALES

	Thumb		Thumb	Index		Long		Ring		Little	
	R	U	IP	R	U	R	U	R	U	R	U
Males	100	100	60.5	39.8	0.3	0.0	0.0	0.0	0.3	1.7	77.6
Females	100	100	65.7	41.3	0.0	0.4	0.0	0.4	0.0	2.6	81.3
TOTALS	100	100	62.7	40.5	0.2	0.2	0.0	0.2	0.2	2.1	79.2

the final hairing, and before the appearance of menstruation.

SESAMOIDS OF THE HAND

It has previously been shown that the sesamoid anlagen are more numerous in the fetus than the definitive structures in later life. We assume that there is originally in the human hand a pair of sesamoids at each metacarpophalangeal joint, although not all have been observed in a single instance. In 299 male and 230 female hands the results in Table II were obtained, with each sesamoid anatomically designated radial or ulnar for convenience.

From the findings given in Table II, it is apparent that the sesamoids in the female hands are slightly more prevalent, but there is no significant difference. Kassatkin's[16] figures are in general agreement, with the incidence of the sesamoids of the females about 10 per cent higher in the index and little fingers.

(a) *Thumb.* In the reported series all radial and ulnar sesamoids or 100 per cent were found. Pfitzner[22] reported 99.9 per cent for the radial and 100 per cent for the ulnar. Bizarro[2] found that in 112 cases the metacarpophalangeal sesamoids of the thumb were missing in 2 instances, a percentage of 98.2. Kassatkin[16] in 1,096 hands studied, either by dissection or roentgenography, reported their presence as 100 per cent.

The sesamoids of the thumb may show bipartition. Pfitzner found this 3 times. Inge and Ferguson[14] studied 200 hands, and reported bipartition of the radial or ulnar sesamoid in 6 per cent of cases. They believe that, because these bones are not well seen in routine roentgenograms, the incidence is greater. In the 529 hands of this series, only 2 cases showed possible partition. Bizarro[2] was unable to find any evidence of bipartition of the pollex sesamoids.

In this series 62.7 per cent of cases had a sesamoid bone present at the interphalangeal joint of the thumb. This is in agreement with other authors. Pfitzner found that the interphalangeal sesamoid was rarely bipartite. Bizarro found a double interphalangeal sesamoid in one case, and I observed this in one case in the 529 hands reviewed.

In Table III the comparative findings of

Table III

PERCENTAGE DISTRIBUTION OF SESAMOID BONES IN THE HAND AS REPORTED BY THESE AUTHORS

	Thumb		Thumb	Index		Long		Ring		Little	
	R	U	IP	R	U	R	U	R	U	R	U
Pfitzner[22]	99.9	100	72.9	47.8	0.1	0.0	0.0	0.0	0.1	2.3	82.4
Fawcett[7]	100	100	68.5	55.2	0.0	0.0	0.0	0.0	0.0	0.0	71.0
Bizarro[2]	98.2	98.2	22.3	64.2	0.0	5.3	0.0	0.0	7.1	0.0	44.6
Kassatkin[16]	100	100	m-76.3 f-86.5	55.8	0.3	3.1	0.1	0.6	0.5	4.9	77.00

TABLE IV

PERCENTAGE ARRANGEMENTS OF SESAMOID COMBINATIONS OF THE HAND IN 529 CASES

	Thumb		Thumb	Index		Long		Ring		Little		Per Cent
	R	U	IP	R	U	R	U	R	U	R	U	
1	*	*	*	*							*	26.1
2	*	*	*								*	24.4
3	*	*									*	16.4
4	*	*	*								*	9.6
5	*	*										9.6
6	*	*	*									8.1
7	*	*	*	*						*	*	1.5
8	*	*	*	*								1.1
9	*	*		*								0.9
10	*	*	*					*			*	0.2
11	*	*	*	*		*					*	0.2
12	*	*		*	*						*	0.2
13	*	*	*	*	*					*	*	0.2
14	*	*	*	*	*						*	0.2
15	*	*	*			*						0.2
16	*	*	**	*	*						*	0.2
17	*	*	*							*		0.2
18	*	*	*						*			0.2
19	*	*		*						*	*	0.2
20	*	*			*						*	0.2

other authors in the literature are given in relation to the reported series.

The percentage combinations that the sesamoids most often assumed, in descending order of frequency are given in Table IV.

Worthy of but brief mention are those instances of small sesamoids that appeared in the index, long and little fingers respectively in which the lumbrical or interosseus tendons appeared to be the site of attachment. In these locations these small sesamoids appeared at the distal margin of the metacarpophangeal joint, just proximal to the base of the proximal phalanx in the area of the tendinous attachments of these muscles.

In a few cases, small osteosclerotic areas appeared in the anteroposterior view of heads of metacarpals and phalanges. Careful inspection of the lateral view showed them not to be sesamoids, but intracortical condensations. The reason for their appearance is unknown.

With the exception of the sesamoid associated with the interphalangeal joint of the thumb, the interphalangeal joints rarely have sesamoid structures.

TABLE V

PERCENTAGE DISTRIBUTION OF SESAMOID BONES IN THE FOOT

	Hallux		Hallux	2nd Toe		3rd Toe		4th Toe		5th Toe	
	T	F	IP	T	F	T	F	T	F	T	F
Males	99.7	100	14.3	2.1	0.0	0.3	0.0	0.7	0.0	9.8	0.7
Females	100	100	25.0	1.8	0.0	0.0	0.0	0.4	0.0	7.1	0.0
TOTALS	99.8	100	19.0	2.0	0.0	0.2	0.0	0.6	0.0	8.6	0.4

TABLE VI

PERCENTAGE DISTRIBUTION OF SESAMOID BONES IN THE FOOT AS REPORTED BY THESE AUTHORS

	Hallux		Hallux	2nd Toe		3rd Toe		4th Toe		5th Toe	
	T	F	IP	T	F	T	F	T	F	T	F
Burman and Lapidus[5]	100	100	13.1	3.4	0.0	0.4	0.0	0.7	0.0	16.3	2.9
Pfitzner[22]	100	100	50.6	1.6	0.0	0.0	0.0	0.0	0.0	6.2	5.5
Bizarro[2]	100	100	5.0	1.0	0.0	0.0	0.0	2.0	0.0	10.0	0.0
Kassatkin[16]	100	100	m-53.3 f-57.8	4.2	0.2	0.7	0.0	1.4	0.6	12.2	10.1

SESAMOIDS OF THE FEET

The embryology and anatomy of the sesamoids of the great toe has previously been discussed. The comparative time order appearance of ossification centers in the sesamoids of the flexor hallucis brevis as given by Francis[9] is shown in Figure 2.

In 286 male and 224 female feet, the results in Table V were obtained, with each sesamoid anatomically designated tibial or fibular for convenience.

These figures are in general agreement with those of other authors, with the exception of the interphalangeal sesamoid of the hallux. This may be due to the fact that the roentgenograms reviewed were sometimes inadequate for an accurate evaluation of the phalangeal structures. In Table VI the comparative findings of other authors in the literature are given in relation to the reported series.

Kassatkin[16] reported the observation of 5 cases in which there were sesamoids beneath each metatarsal head; a maximum of 8 in one case, distributed as follows: two beneath the heads of the first, fourth and fifth toes, and one on the medial or tibial side of the second and third toes. Other authors including Lapidus[19] and Patterson[21] report cases showing the presence of the rarer sesamoid bones. Interphalangeal sesamoids have been reported by Bizarro and Pfitzner, but their incidence is rare.

The percentage combinations that the sesamoids most often assumed, in descending order of frequency, are given in Table VII.

TABLE VII

PERCENTAGE ARRANGEMENTS OF SESAMOID COMBINATIONS OF THE FOOT IN 510 CASES

	Hallux		2nd		3rd		4th		5th		Hallux	Per Cent
	T	F	T	F	T	F	T	F	T	F	IP	
1	*	*										72.2
2	*	*									*	17.1
3	*	*							*			5.9
4	*	*							*		*	1.6
5	*	*	*						*			0.8
6	*	*					*		*			0.6
7	*	*	*									0.6
8	*	*	*						*			0.4
9	*	*								*		0.2
10	—	*										0.2
11	*	*			*							0.2
12	*	*								*	*	0.2
13	*	*	*								*	0.2

Congenital absence of the hallux sesamoids is extremely rare. In reviewing the literature only 3 cases of congenital absence of the tibial sesamoid bone of the great toe have been reported. Inge[13] reports 2 cases, and Lapidus[18] one. One case in this series of 510 feet showed congenital absence of the tibial sesamoid bone. This unusual anomaly is evidently the fourth such case to be reported and is illustrated in Figure 3. Unfortunately the roentgenogram of the opposite foot was absent.



Fig. 3. (SS 2208) White male, aged twenty-two years, eleven months. Congenital absence of tibial sesamoid of the left great toe.

In 7 instances, in the 510 feet reviewed, there were sesamoids at the tibial side of the fifth toe, and these appeared to be situated in the intrinsic musculature. This view is supported by Lapidus.[19] In 8 cases, there was present a small accessory sesa-



Fig. 4. (SS 1919) White male, aged eighteen years, eight months. Bipartition of tibial sesamoid.

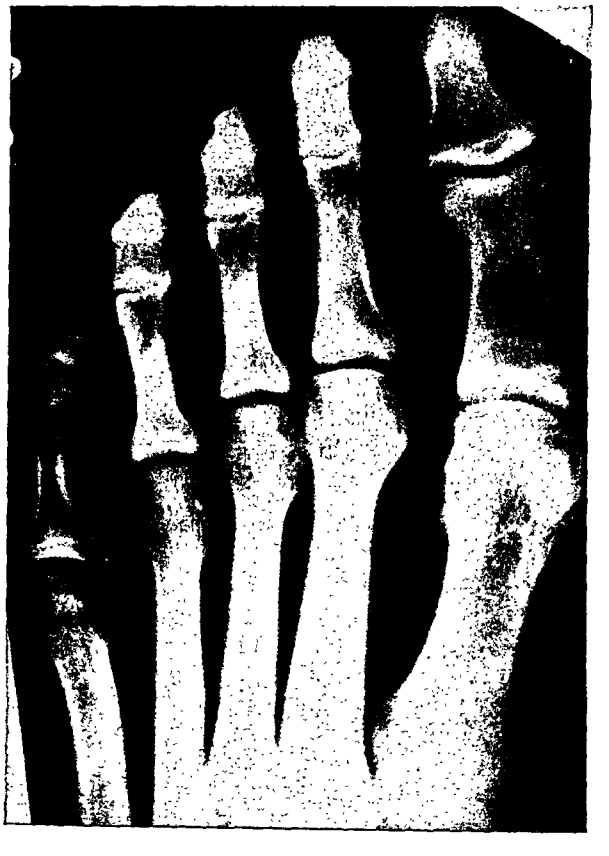


Fig. 5. (SS 3519E) White male, aged eighteen years, eleven months. Bipartition of fibular sesamoid.



Fig. 6. (SS 849) White female, aged eighteen years, ten months. Bipartition of tibial and fibular sesamoids.



Fig. 7. (SS 2210) White male, aged twenty-one years, eleven months. Bipartition of tibial and fibular sesamoids.



Fig. 8. (SS 4118B) White male, aged fourteen years. Bipartition of tibial sesamoid.

moid at the medial margin of the hallux interphalangeal joint. This was associated with a regular middle sesamoid in 3 cases and appeared alone in 5 instances.

BIPARTITION OF SESAMOIDS

Because the anatomical location of the metatarsal sesamoid bones of the great toe renders them particularly liable to trauma, it is especially important that bipartition of the sesamoids be recognized. This is of medicolegal interest, and occasionally is the basis for compensation claims. It has been shown by various authors that partition of both the tibial and fibular sesamoids does occur. Examples of bipartition of the medial or tibial sesamoid is shown in Figure 4, the fibular in Figure 5, and of both in Figures 6 and 7.



Fig. 10. (SS 4118D) White male, aged sixteen years. Beginning fusion of partite centers.

Lapidus[20] demonstrated bipartition of the second toe tibial sesamoid bilaterally, and bipartition of the left third toe sesamoid. Undoubtedly others do occur.

During growth an ossicle usually appears simultaneously in each tendon. Occasionally ossification in one tendon may precede that in the other, and when this occurs the fibular usually ossifies first. In 100 boys at 15 years, Francis[9] found a double sesamoid in 26 of the tibial sesamoids, and 7 in the fibular. One boy showed a double sesamoid in each position. Of 90 girls in the 15 year age group, 27 showed division of the tibial sesamoid and only one of the fibular sesamoid.

Ossification may occur from multiple centers which may, or may not, unite subsequently. Several authors refer to failure

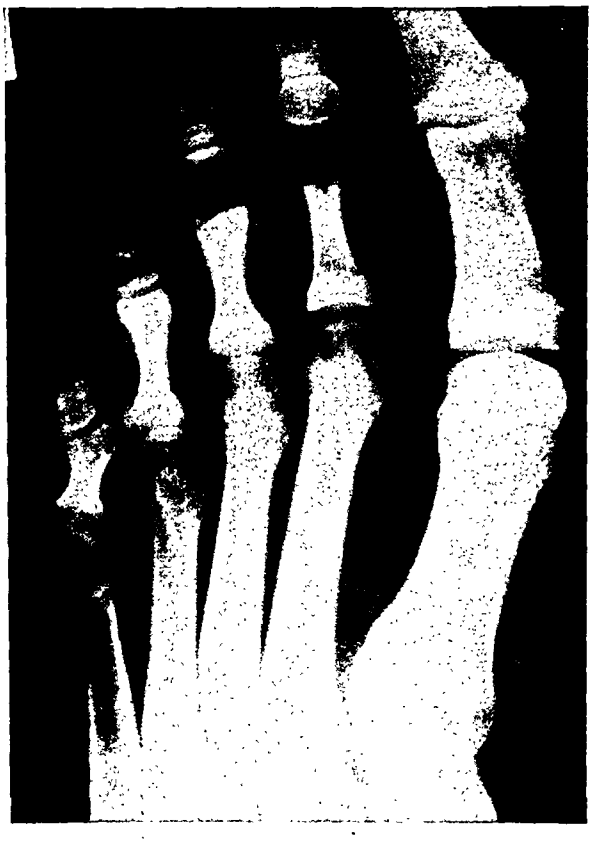


Fig. 9. (SS 4118C) White male, aged fifteen years. Growth of sesamoids with bipartition still present.



Fig. 11. (SS 4118E) White male, aged seventeen years. Advance of fusion of partite centers.



Fig. 12. (SS 4118F) White male, aged eighteen years. Fusion nearly complete and partition is no longer present.

Table VIII

FROM INGE AND FERGUSON, SHOWING THE DECREASE OF BIPARTITE SESAMOIDS AS AGE INCREASES, AND THE INCREASE OF FUSED CENTERS AS AGE INCREASES

Age	No. of Cases	No. of Feet Examined	No. of Feet Showing Divided Sesamoids	No. of Feet Showing Sesamoid Developed in Two Parts Now United
10	45	90	18	0
15	49	98	21	8
20	45	90	14	12
25	41	82	8	8
30	51	102	9	32
35	50	100	10	40
40	44	88	8	48
45	36	72	4	12
50	33	66	4	28
55	24	48	4	0
60+	15	30	1	28

of union of these multiple centers as congenital division. Bipartition, tripartition and quadripartition are probably better descriptive terms and are anatomically more accurate. That this is a failure of fusion is shown by the serial roentgenograms (Fig. 8 to 12) taken from the files of the Brush Foundation. It is apparent that ossification developed from two centers in the tibial sesamoid of the great toe, and, whereas bipartition can be demonstrated at 14 years, it is impossible to make that diagnosis at 18 years as fusion of the two centers has taken place.

Supporters of this contention are Inge and Ferguson[14] who showed that the incidence of bipartition of the hallux sesamoids decreased as age increased. This is shown in Table VIII taken from those authors.

In this series of 510 feet the incidence of bipartite sesamoids was carefully noted. Partitions of more than two centers have been included in the following figures. There is no statistical significant difference in the two sexes and this is shown in Table IX.

These figures are in general agreement

Table IX

PERCENTAGE OF PARTITE SESAMOIDS OF THE FEET AS TO SEX

	Hallux Sesamoids	
	Tibial	Fibular
286 males	13.6	2.8
224 females	17.9	1.8
TOTALS	15.5	2.4

Table X

PERCENTAGE OF PARTITE SESAMOIDS AS GIVEN BY THESE AUTHORS

	Hallux Sesamoids	
Author	Tibial	Fibular
Kewenter[17]	30.6	1.3
Bizarro[2]	5.0	0.0
Burman and Lapidus[5]	7.2	0.6
Powers[23]	13.0	1.0
Francis[9]	27.8	4.2

with other authors whose incidence of partite sesamoids is shown in Table x.

Kewenter,[17] in an excellent monograph, discusses the sesamoids of the big toe in 800 cases. He found no partition in 66.1 per cent of his cases; 268 cases, or 33.3 per cent, showed one division only. Of the 268 cases, 146, or 18.25 per cent, were bipartite. In 122 cases there were two or more unilateral separations. There was bilateral division of the medial sesamoid in 13.5 per cent of cases. There was division of the fibular sesamoid

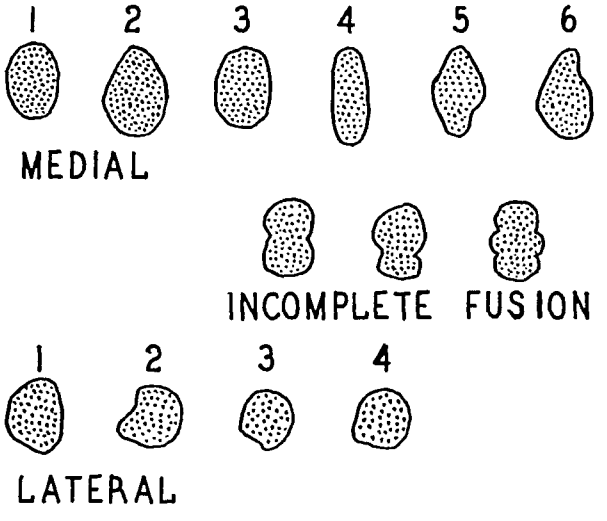


Fig. 13. (Redrawn from Kewenter.[17]) Normal sesamoids of the great toe in descending order of frequency of appearance.

in 1.3 per cent of cases. This series is of the left foot alone and comparison with Kewenter cannot be made. Two of these cases showed bipartition of both the tibial and fibular sesamoids. They are shown in Figures 6 and 7.

The diagrams (Fig. 13 and 14) taken from Kewenter's monograph[17] show the appearance of normal and partite sesamoids of the most common forms in decending frequency of appearance.

SURGICAL CONSIDERATIONS

The surgical importance of the sesamoids has been emphasized by Bizarro,[3] Lapidus,[20] Inge and Ferguson[14] Gottlieb,[11] Sinberg,[25] Scott,[24] and others. Fracture of the great toe sesamoids is not common, and that of the thumb is rare.

The tibial sesamoid is more frequently the site of fracture than the fibular, due to the anatomical location of the tibial directly beneath the head of the first metatarsal. The fibular lies to the side and is partially protected, although several cases of fracture of the fibular sesamoid have been reported by Bizarro[3] and others.

Sinberg[25] reported a fracture of a sesamoid of the thumb in a nurse, with subsequent healing adequately demonstrated roentgenographically. Since fractures of the pollex sesamoids are extremely rare the remainder of this discussion will be related to the injury of the hallux sesamoids, although the general considerations can be readily applied to the pollex sesamoids.

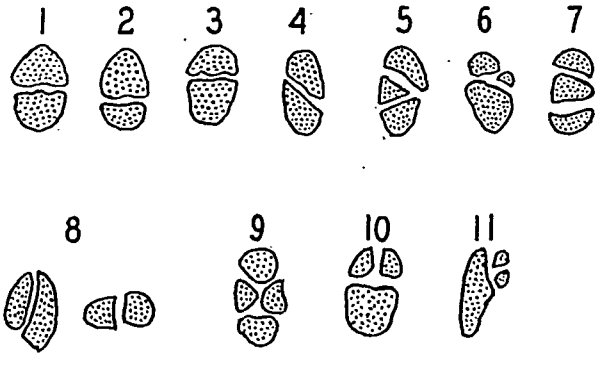


Fig. 14. (Redrawn from Kewenter.[17]) Showing developmental variations of the partite sesamoids of the great toe in descending order of frequency of appearance.

Fracture of the sesamoids is usually the result of direct trauma, although a few cases appear to be due to indirect trauma. There may be associated fractures of the surrounding bones of the foot, especially of the metatarsals and phalanges if a crushing type of injury is encountered.

The differential diagnosis between fracture and trauma to partite sesamoids is important. Direct trauma to a partite sesamoid may result in ecchymosis, tenderness and pain, yet be confined wholly to soft tissue injury. Gottlieb[11] in discussing painful sesamoids states that the cause of the condition may be due to repeated "microtrauma," rather than a single severe injury. He offers as evidence the fact that most of his cases were seen in women who have worn high-heeled shoes for many years

and whose occupation called for prolonged walking or standing.

Powers[23] believes that, due to the anatomical location of the sesamoids and their developmental variations, they are frequently the seat of local pain and tenderness following injuries elsewhere in the foot.

In all suspicious injuries, roentgenograms should be made. They should be taken with the toe in marked dorsiflexion, the rays being in the frontal plane. Both feet should be examined as developmental variations are frequently bilateral.

The criteria for fracture of the sesamoids are as follows:

1. Irregular and unequal separation of the affected sesamoid with the fragments possibly being serrate.

2. Evidence or attempt at healing by the formation of callus in subsequent roentgenograms.

3. Absence of similar findings in the roentgenograms taken of the opposite side.

4. If operative removal has been done, gross and microscopic pathological evidence of fracture.

SUMMARY AND CONCLUSIONS

1. A historical, embryological and anatomical survey of the sesamoids of the hands and feet has been presented.

2. Ossification of the sesamoids of the hands and feet has been reviewed and the two year developmental lag of the male has been stressed.

3. The sesamoid structures in 529 adult hands and in 510 adult feet have been analyzed with regard to sex distribution; findings of negligible difference have been presented.

4. Partition of the sesamoids has been discussed and evidence for fusion of multiple centers has been shown.

5. A case of congenital absence of the left tibial sesamoid of the great toe is given.

6. Differential diagnosis between fracture and partition of the sesamoids is emphasized and criteria for fracture are established.

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OCCUPATIONAL CALCAREOUS PERITENDINITIS OF THE FEET

A CASE REPORT

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THE purpose of this paper is to present an unusual case of calcareous peritendinitis of the peroneal tendons of both feet. An attempt will be made to evaluate the findings in the light of the patient's occupation.

It is believed that no similar case has been previously reported in the literature. Roberts,[3] reporting 50 cases of bursitis of the foot in 1929, mentions only the head and base of the fifth metatarsal as sites for the formation of adventitious bursae on the outer aspect of the foot. However, such bursae may conceivably occur at any point along the outer aspect of the foot where pressure and friction are constantly applied. Inflammatory and degenerative changes may lead eventually to the deposition of calcium salts in the wall of the bursa, in the adjoining tendon sheath, or in the tendon itself—the pathological mechanism being similar to that so commonly seen in the bursae and tendon cuff of the shoulder.[2]

CASE REPORT

G. G., male, white, aged thirty, house-painter, awoke on the morning of December 1, 1946, with pain over the outer aspect of his left foot. The pain rapidly became quite severe, and he consulted his doctor, who sent him to the

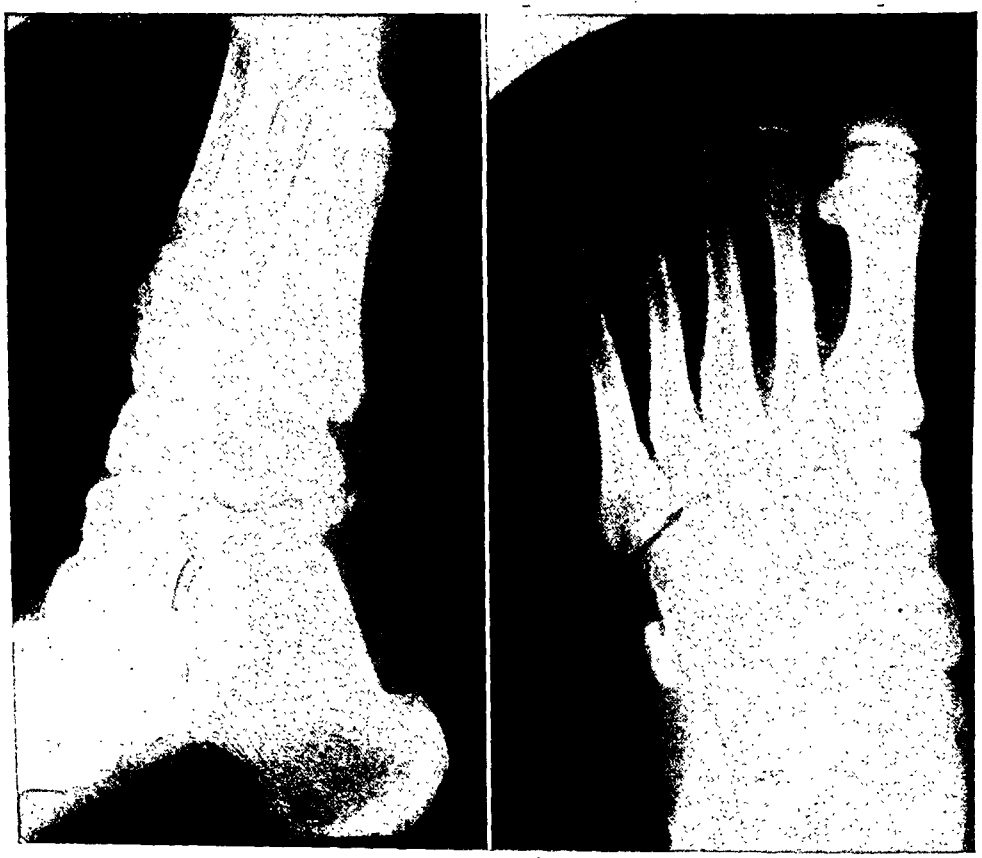


FIG. 1. Left foot, showing the original appearance of the calcification on the lateral aspect of the calcaneocuboid articulation.

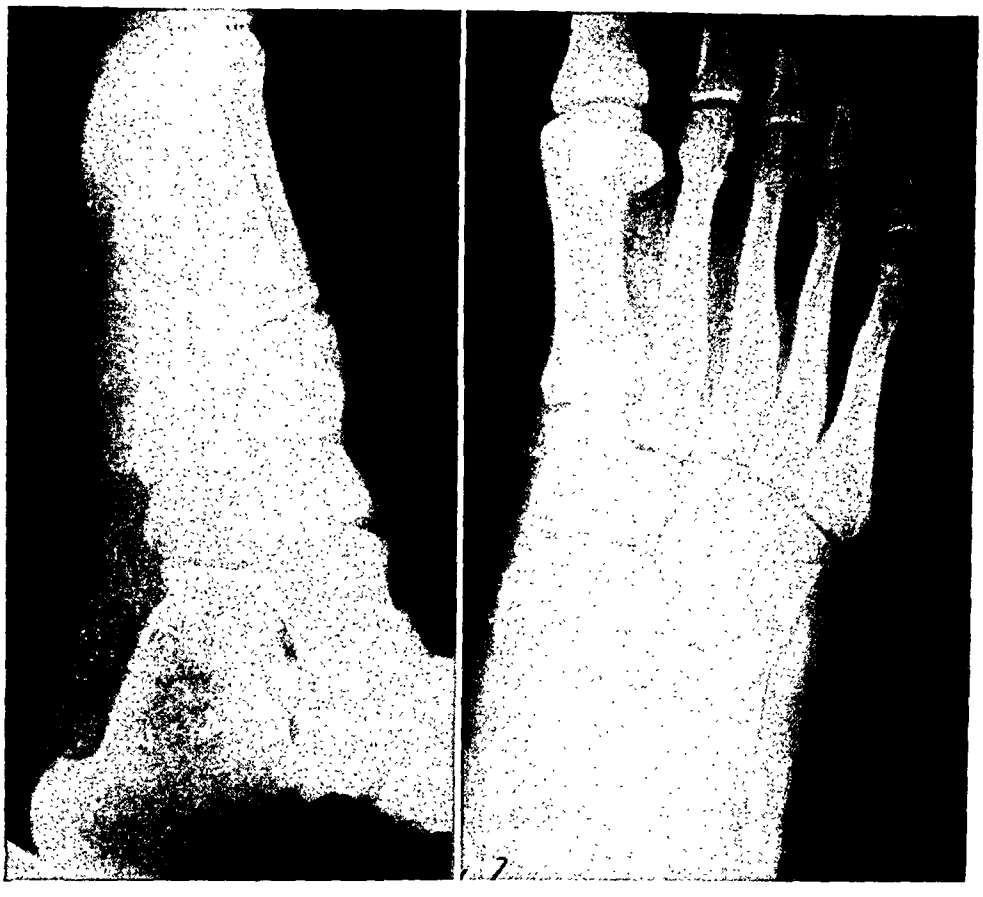


FIG. 2. Right foot, showing a similar calcified deposit.

Newton-Wellesley Hospital for a roentgen examination of his left foot (Fig. 1), which revealed a fragmented calcific deposit just lateral to the calcaneocuboid articulation. This unusual finding prompted examination of the other foot, which showed an almost identical calcified mass (Fig. 2). The patient was unable to bear any weight on his left foot, and the involved area was hot and swollen. His doctor strapped his foot and prescribed rest, and the pain and swelling subsided somewhat. A week later, however, the same symptoms appeared with greater severity in the other foot, and he was admitted to the Cushing Veterans Administration Hospital.

The general physical examination was essentially negative. The temperature, pulse and respiration were normal. In the right foot there was extreme tenderness over the lateral aspect of the cuboid. The skin was red and the tissues slightly edematous. In the left foot, definite point tenderness was elicited over the lateral aspect of the cuboid. The laboratory findings were normal, with the exception of the sedimentation rate, which was raised to 29 mm.

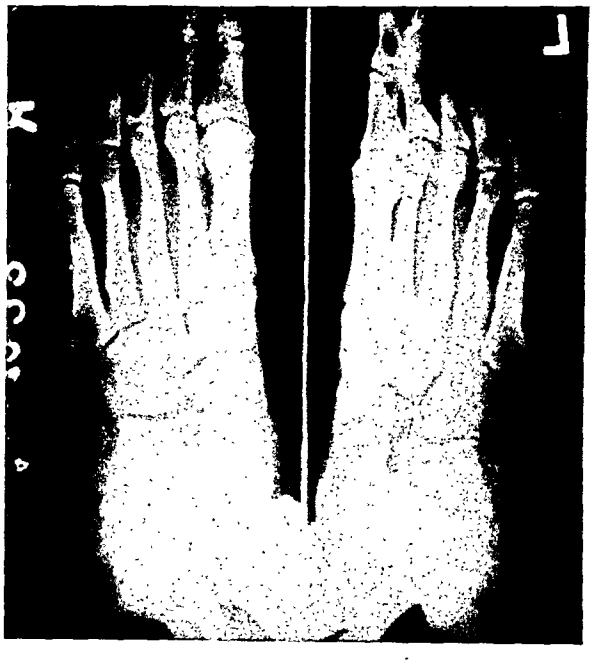


FIG. 3. Appearance of the calcified deposits four weeks following operation on the right foot. The calcification is seen to follow the course of the peroneal tendon sheath; this is particularly evident in the left foot.

(normal 8–10 mm., Wintrobe); this returned to normal in a week.

On December 19, under local anesthesia, a No. 21 gauge needle was passed into the sheath of the peroneus longus and brevis over the calcaneocuboid articulation of the right foot. The sheath was infiltrated with novocaine, and the needle was then passed beneath the sheath toward the cuboid. In this area a grating sensation was transmitted from the tip of the needle. Two or three drops of material, white in color and of the consistency of toothpaste, were obtained from this area, which was then approached with needles of varying gauge. No successful irrigation was carried out, and no further material could be obtained. Culture of the aspirated material produced no growth in seventy-two hours.

Two weeks later the patient was asymptomatic except for slight tenderness over the lateral aspects of both feet in the region of the cuboids. Roentgen examination about this time showed that the calcification was distributed along the course of the peroneal tendon sheath on both sides, though there was a marked reduction in the total amount present, particularly in the right foot (Fig. 3).

The patient was discharged six weeks after admission, apparently cured. He was seen again at the Newton-Wellesley Hospital in August, 1947. Roentgen examination at this time showed only a few tiny flecks of residual calcification near both cuboids (Fig. 4). The anterior surfaces of the tibiae showed no essential variation from the normal. (This latter examination was made at the suggestion of Dr. Merrill C. Sosman, who has noted proliferative changes in the periosteum of the anterior surfaces of the tibiae in house-painters, due to the pressure of the lower legs against the ladder rung.)

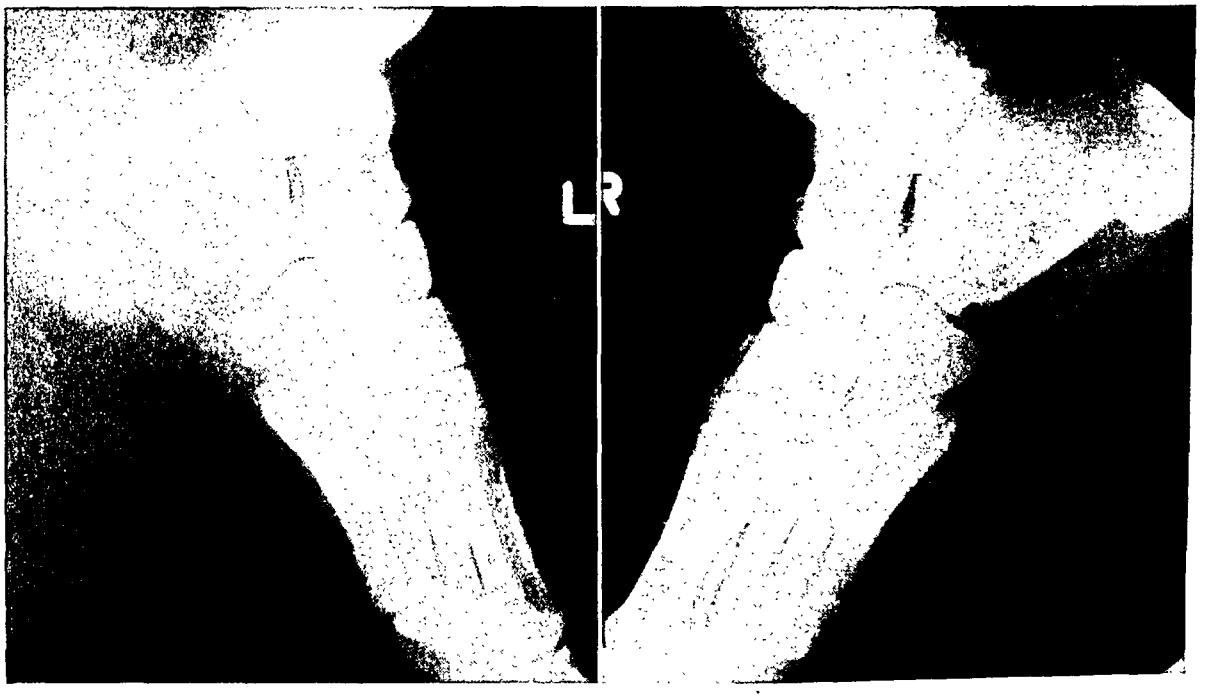


Fig. 4. Eight months later the calcification is barely visible as a few tiny flecks near each cuboid.

The occupational aspects of this condition were closely investigated by careful questioning of the patient. For nine years of his life, from 1935 to 1944, he had spent an average of at least four hours a day on ladders of the long narrow-runged type. From 1944 till his discharge from the Army in March, 1946, he had not been engaged in this type of work. Between March, 1946, and the onset of his illness his jobs had involved ladder-climbing on only two occasions, the last being just two days prior to the acute episode. On that day he had spent eight hours working on a ladder. At no time in the past had he ever experienced pain of a similar nature in his feet.

The patient was asked to simulate his accustomed stance while working on a ladder,

using as a convenient model the side-bar between the legs of a chair. It was found that, as he braced himself against the legs of the chair, the point of pressure corresponded exactly to the original areas of tenderness and calcification.

The patient has had no recurrence up to this date, and has pursued his work in a normal manner—though he has been careful to refrain from working on ladders.

DISCUSSION

Anatomy (Fig. 5). The tendons of the peroneus longus and brevis muscles are invested by a common synovial sheath which begins at the back of the external malleolus and divides as it approaches the peroneal tubercle of the calcaneum. The upper portion is prolonged on the peroneus brevis tendon almost to its insertion at the base of the fifth metatarsal; the lower portion ensheaths the peroneus longus (with or without interruption at the lateral side of the foot) across the sole of the foot to its insertion in the first cuneiform and base of the first metatarsal.[1] These tendons are the chief evertors, and the tendon of the peroneus longus moreover forms a most important sling in the middle of the arch of the foot.

When standing on the rung of a ladder, the average person automatically balances himself by bracing his feet against the sides of the ladder, so that the point of pressure on the lateral aspect of the foot coincides with the cuboid tuberosity over which the peroneal tendons pass. The tendons are thus pressed closely up against a bony prominence during the very time that they are being stretched by the synergic action of the peroneal muscles, which are, in conjunction with the invertors of the foot, operating to maintain a constant balance. It is believed that this unusual occurrence of pressure by two unyielding surfaces on a tendon relatively immobilized by its functional tautness offers a reasonable explanation for the development of the condition described in this paper. It must be assumed that bruising and irritation of the soft tissues was followed in the course of time by a localized degeneration and the deposition of calcium salts. The tendons and tendon sheaths have a lining membrane similar to the synovial membrane of joints

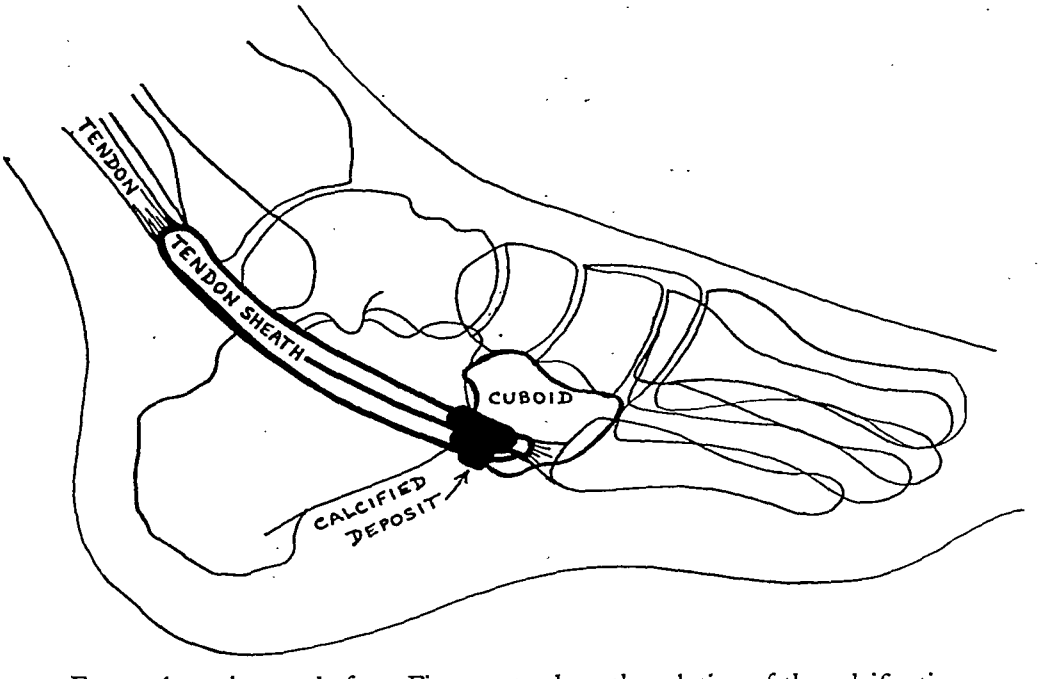


Fig. 5. A tracing made from Figure 1 to show the relation of the calcification to the peroneal tendon sheath.

and bursae, and it is well known that post-traumatic degeneration of this specialized tissue is frequently followed by calcification in the subsynovial tissue strata.

From an anatomical point of view, it must be admitted that there are three areas where the calcification may have occurred in this particular case: in the tendon itself, in the tendon sheath, or in the wall of an adventitious bursa formed between the tendon sheath and the cuboid. The course of the calcification as seen in Figure 3 tends to rule out the last possibility, but the exact anatomical location must remain a controversial point in the light of our present meager evidence.

The most logical sequence of events, in the light of the patient's history, can probably be reconstructed as follows: Repeated slight trauma over a period of several years led to the calcification seen at the time of the first examination. It is likely that the sudden new injury was the causative factor in producing the acute inflammatory response which occurred in the areas where the large calcium deposits had been lying, relatively quiescent, for several years. Further discussion of this interesting problem is beyond the present scope of this paper. An investigation is now being carried on among a large group of individuals whose occupation necessitates work of the same nature as that engaged in by the patient in this case history. These findings will be reported at a later date.

SUMMARY

(1) An unusual case of calcareous peritendinitis of the peroneal tendons of both feet is presented.

(2) It is suggested that this is an occupational disease which has not been previously reported as such, and which may possibly occur more frequently than is realized in house-painters and in those who spend a great deal of their time on narrow-runged ladders.

ACKNOWLEDGMENTS

Part of the case history was obtained, with the kind permission of Dr. R. E. Carroll, from the case records of the Cushing Veterans Administration Hospital. The roentgenogram reproduced in Figure 3 was borrowed from the Department of Radiology of the same hospital, with the kind permission of Dr. D. Kornblum.

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Vol. 61, No. 4

KAPOSI'S SARCOMA

REPORT OF TWO CASES*

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KAPOSI'S sarcoma, or multiple idiopathic hemorrhagic sarcoma, is an unusual disease among adults in America. Two cases are presented that represent the acute fulminating and the chronic aspects of the disease.

REPORT OF CASES

CASE I. F. McG., an American born white male, aged fifty-eight, with a twelve year history of skin lesions.

The disease began seven years prior to the first admission, August 3, 1942, when a small red area developed on the nose. Since, similar lesions have appeared on the right foot and left ankle. On examination there were numerous papillary growths, dark in color, with other areas of blue demarcation.

The patient was referred to the X-ray Therapy Department for treatment of the lesions of the medial surface of the right foot, the left ankle, lower left leg and a developing lesion of the sole of the right foot. Over a two month period he received 3,840 r to the lesions of the right foot and 3,200 r to those of the left ankle. Additional therapy was given to the sole of the right foot and to the original right foot area and a recurrence at the base of the fourth right toe. A total of 12,000 r, measured in air, was given to the lesions of the feet and ankles with a poor response to the irradiation.

In June, 1943, the patient was again admitted complaining of swelling in the throat of four to five months' duration which caused difficulty in swallowing, and nausea. During the past eight years a gradual loss of 17 pounds had occurred. No other symptoms referable to the gastrointestinal tract were present. There was an additional lesion on the penis just above the coronal sulcus. An irregular blue-red mass was removed from the anterior surface of the uvula. Microscopically, the specimen revealed the connective tissue to be infiltrated by a very vascular tissue, the cells of which were mainly spindle shaped with elongated dark staining nuclei. Numerous thick-walled small blood vessels were noted with intimal proliferation and some ecchymosis into the tissue and under the epithelium of the mucosa. Diagnosis: Multiple hemorrhagic sarcoma.

The third admission, May, 1944, was for marked swelling of the right leg to the knee and secondary infection. After treatment with warm saline soaks, elevation of the leg and sulfadiazine by mouth, a mid-thigh guillotine amputation was performed. Microscopically the sections revealed a fibroblastic growth in the subcutaneous tissues with cells of the oat cell variety with long thin nuclei and interweaving among themselves in a true sarcomatous arrangement. The tumor was quite vascular and in places was almost mesh-like from the number of small blood vessels present. Diagnosis: Kaposi's sarcoma.



FIG. 1. Case 1. Lesion of the sole of the right foot.

The last admission, January, 1945, was for treatment of a secondarily infected tumor of the left third toe. Since the amputation of the right leg, the patient had gained 20 pounds in weight and had no symptoms referable to the gastrointestinal tract.

When the patient was last seen in February, 1947, there were extensive lesions of the left ankle and foot, of either arm and one small reddened area of the amputation stump. He had slowly lost weight but otherwise his condition was fairly satisfactory and his hemoglobin

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Fig. 2. Case I. Lesions of the left foot and lower leg.

and red blood cell count remained within normal limits throughout the disease.

Case II. G. M., an Italian born, white male, aged fifty-seven, with an eight month history of the disease.



Fig. 3. Case II. Original lesion of the tonsillar area.

In July, 1946, he began to have difficulty in swallowing and was seen by several physicians who gave him various treatments for a tumor-like mass of his throat. One removed a small tumor from the tonsillar area which bled considerably during and after the operation.

A large sessile tumor was removed from the left tonsillar area in November, 1946. Complete examination of the throat at that time revealed



Fig. 4. Case II. Tumor mass removed from the tonsillar area.

multiple bluish hemorrhagic lesions filling the vallecula and the base of the epiglottis. The palm of the left hand also had bluish hemorrhagic lesions and the dorsum was edematous. It was believed that the swelling of the hand was due to a mass in the supraclavicular and axillary areas. Large inguinal nodes were present with considerable edema of the feet and legs.

The patient was given roentgen therapy over the supraclavicular and axillary areas resulting in slight reduction in the size of these nodes and improvement in the swelling of the left hand.

Shortly after the completion of the roentgen therapy, the patient began to complain of nausea and almost constant abdominal pain.

He passed several tarry stools. A marked anemia was present with a hemoglobin of 40 per cent. A gastrointestinal series on December 19, 1946, showed multiple papillary or polypoid lesions of the small intestine.

The patient has continued to have gastrointestinal bleeding and has received six transfusions during the past two months. The hemoglobin has continued to remain about 50 per cent. During this period he has received daily treatments with varying dosages of mustard gas with little or no response.



Fig. 5. Case 11. Lesions of the palm of the left hand.

When last seen during the second week in February, 1947, the patient's condition had rapidly become worse. He continues to have gastrointestinal bleeding. Enlargement of the liver with the development of ascites had occurred.

This interesting condition was first described by Kaposi in 1872, who found histopathologically a small cell sarcoma. He thought it was a general disease because it began at the same time on both the hands and feet.[8]

The disease is one of geographic rather than racial incidence, chiefly affecting the inhabitants of central and southeastern Europe. It is common in northern Italy Russia, Poland, and "is relatively common in New York City and other cosmopolitan urban centers."[10] The highest incidence is in the age groups fifty to seventy and is rare in children "less than one percent of the reported cases occurring under the age of ten years."[1] It is uncommon in Negroes. The



Fig. 6. Case 11. Lesions on the dorsum of the left hand.

condition is about twenty times more common in males than females.

The etiology is unknown. One group believes that the condition is a true neoplasm and the other that it is an infectious granuloma. Investigations were done by Choisser and Ramsey[2] based on the proposition that "if the disease were of infectious origin it should be possible to isolate the causative organism from the lesions, to cultivate it and to transmit the disease to experimental animals." These writers came to the conclusion that Kaposi's sarcoma is in all "probability a true neoplasm derived from the reticulo-endothelial system and is best described by the term angio-reticulo-endothelioma."

The disease is usually first manifested by skin lesions but cases have been reported in which visceral lesions have preceded the cutaneous manifestations. The lesion usually begins as a reddened macular area on an extremity, most commonly the leg or foot. As the lesion ages it becomes firm, the color gradually becomes bluish and the macules develop into varying sized papules. These changes are easily understood by a comparison of the microscopic appearance of the lesion in its various stages. At first the parenchyma is infiltrated and compressed by a new formation consisting of new blood vessels and a richly cellular connective tissue. There is an increase of the reticulum as demonstrated by the Bielschowsky stain. The reticulum is closely

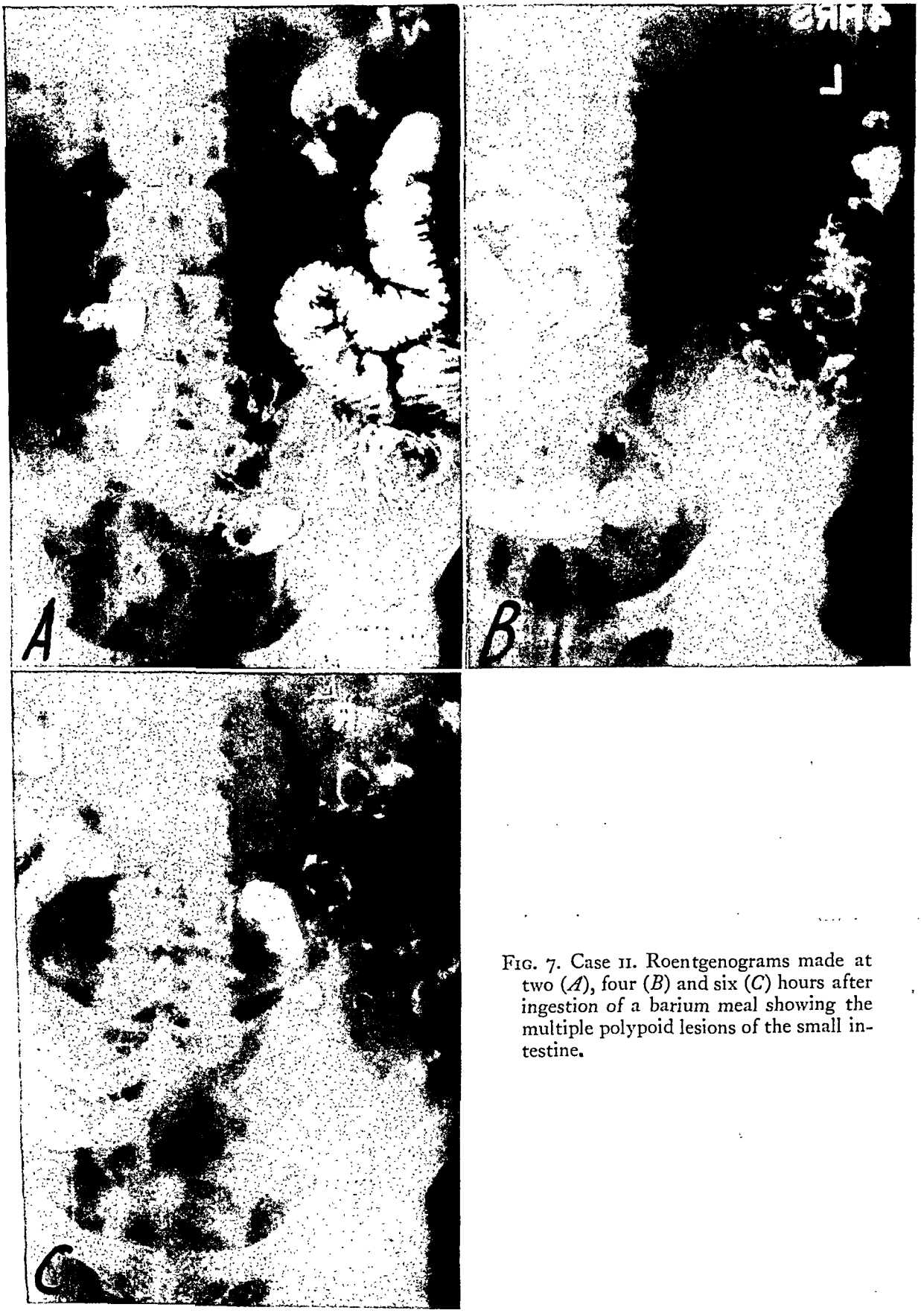


Fig. 7. Case 11. Roentgenograms made at two (*A*), four (*B*) and six (*C*) hours after ingestion of a barium meal showing the multiple polypoid lesions of the small intestine.

associated with new vessels and precedes them in invading partially destroyed parenchyma. As the lesion ages the cellular elements increase and there is stagnation of the blood, and hemorrhage into the surrounding tissues. The endothelial cells seem to change into a fibroblastic type of cell and a marked increase of a richly cellular tissue with large oval or spindle nuclei resembling a young connective tissue is seen. The acute cases show more malignancy in individual cell structure as evidenced by pleomorphism, hyperchromatism, abundance of mitotic figures and embryonic cell types.

Autopsy findings reveal that nearly every organ of the body may be involved by the disease. Lesions in the muscles, though rare, have been reported, particularly in the diaphragm and the intercostal muscles. No lesions have been found in the substance of the brain or spinal cord, but "the dura supposedly has been involved in one reported case."[4]

Ordinarily the course of Kaposi's sarcoma is slow and steadily or intermittently progressive. Old lesions often undergo spontaneous involution. The extent is from eight months to twenty-five years with the average duration being between five and ten years. Death usually occurs from intercurrent infection or infiltration of the lungs, spleen or liver, but the most common occurrence is metastasis to the intestinal mucosa with ulceration and hemorrhage.

Practically all authorities agree that roentgen therapy probably gives the best results in treatment of the disease, but this is palliative. It is the early vascular lesion that usually responds to small doses of low voltage roentgen therapy, while the later type of lesion is much more resistant to treatment. Most of the lesions can be made to disappear with moderately heavy radiation dosage. However, if the patient is young, with a life expectancy of ten to fifteen years, irradiation has not proved to be a very satisfactory method for control of the disease.

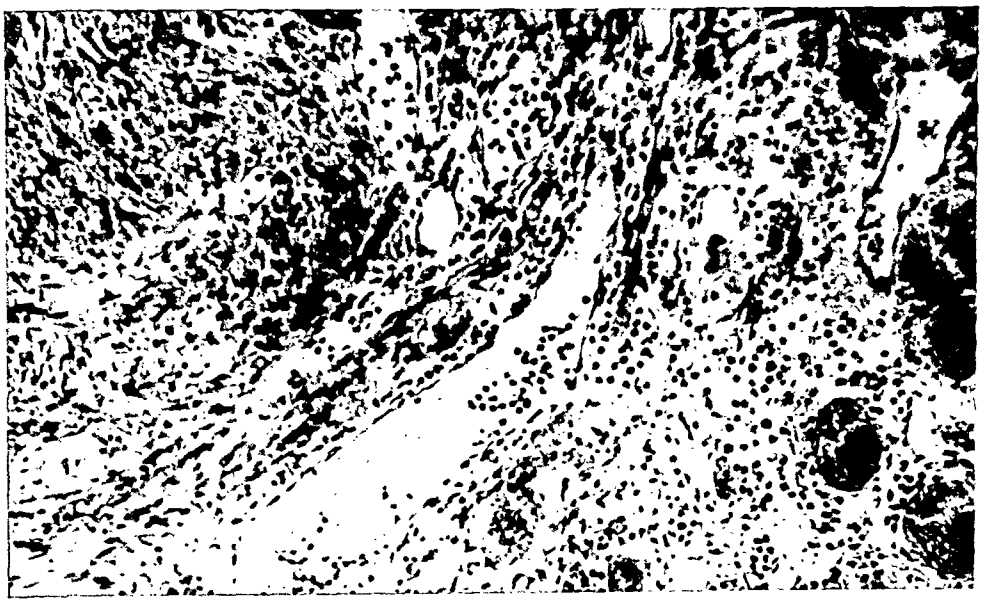


Fig. 8. Photomicrograph of early stage demonstrating rich vascularity, spindle and round cells of the tumor.

The use of radium and radon therapy is not satisfactory because of the numerous lesions and the large areas that have to be treated.

Arsenic has been used either alone or in conjunction with roentgen therapy. It has been administered chiefly by mouth as Fowler's solution, but has been given

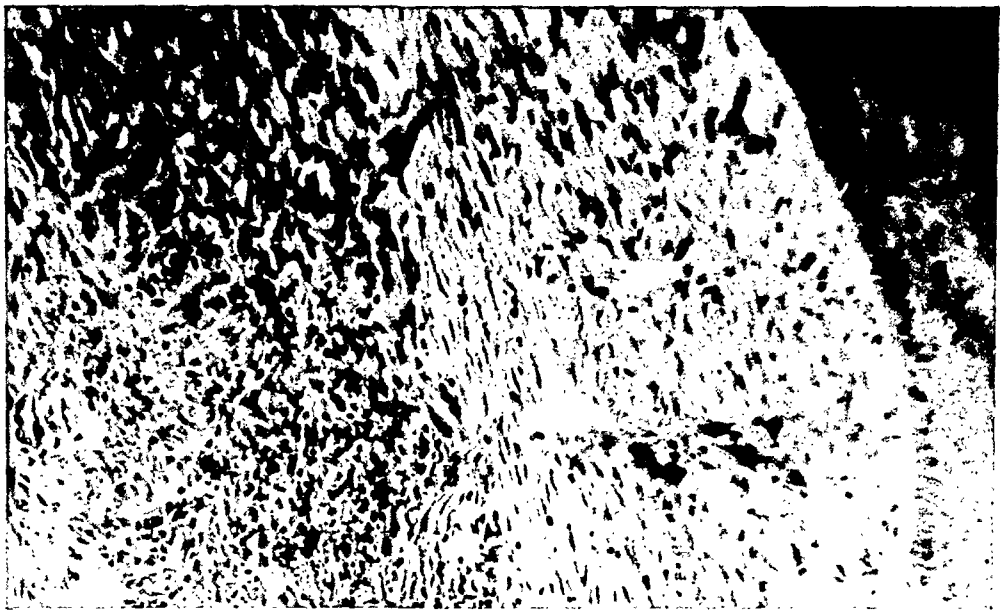


Fig. 9. Photomicrograph of late stage lesion in the dermis revealing compact arrangement of spindle cells and decreased vascularity.

parenterally as well. When used, the treatment should be intensive.

Other methods of treatment which are seldom used are surgery, electrodesiccation and electrocoagulation. Modified mustard gas and the nitrogen mustards are relatively new and their effects have not been proved.

Forman[6] reported a case that showed spontaneous healing.

MacKee and Cipollaro[10] believe "that recurrence, sooner or later, is the rule, and that, while the treatment agent causes involution of the eruption to which it is applied, it has little or no influence on the etiology of the disease and it does not prevent the development of new lesions in various parts of the body."

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VOL. 61, NO. 4

RADIUM THERAPY FOR CARCINOMA OF BARTHOLIN'S GLANDS*

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CARCINOMA of Bartholin's glands (greater vestibular glands) is rare and a poor prognosis is justified should the capsule be perforated by the malignant process. The purpose of this paper is twofold: to note the cases of carcinoma of Bartholin's gland represented in the surgical records of the Mayo Clinic, and to record that judicious radium therapy and roentgen therapy, either or both, are indicated as curative procedures, even after local recurrence and clinical metastasis.

Between January, 1910 and December 31, 1947 inclusive, approximately 700 benign lesions of Bartholin's glands were surgically treated and microscopically studied at the Mayo Clinic: this number included cysts, abscesses and chronic inflammatory conditions. During the same period, 7 primary malignant growths of this gland were found, or an incidence of 1 per cent of all lesions of Bartholin's glands for which operation was performed, which compares closely with the 1.1 per cent quoted by the New York Post-Graduate Hospital group.[28]

Rabson and Meeker quoted Lynch and Maxwell concerning the general frequency of carcinoma of Bartholin's glands: "this tumor is undoubtedly rare, yet the literature does not properly express the frequency, since vulval growths are usually seen by the men in general practice who do not report them and who may be content merely with their removal." It is realized that in a case of squamous-cell carcinoma of Bartholin's gland in which the vulva is infiltrated and the condition has been neglected, the origin of the malignancy cannot be stated. Vulval malignancy is not uncommon.[7] Moore stated that it ranks third among neoplasms of the female genitalia. It may involve Bartholin's gland by direct extension. This eventuality needs to be excluded when referring to true carcinoma of Bartholin's gland.

Spencer listed 13 cases from the world literature, and reported 1 additional case. Falls listed 16 cases from the world literature, and stated that the first report by a resident of the United States of a case which occurred in that country appeared in Kelly's "Operative Gynecology" of 1907, page 253. Falls added a report of 1 case. Rabinovitch estimated the world literature to contain reports of 40 cases and added a report of 1 case. Harer found reports of 30 cases, some of which he considered doubtful. Lyle found reports of 36 cases, 11 from the United States, and reported 1 additional case. Rabson amd Meeker found reports of 56 cases and added 2. Simendinger listed 38 cases from the world literature and added a report of 1 case. Taussig mentioned 9 cases of carcinoma of Bartholin's glands among 155 cases of vulval carcinoma, but gave no detail specifically concerning these cases. Pund and Cole added a report of 1 case. Boughton estimated that the world literature contains about 75 reports of cases, many of which were published with insufficient data. She added a report of 1 case. Hynes reported 1 case. LeDoux stated that 2 cases are on record at Hotel Dieu, New Orleans, and added a report of 1 case which he had observed in twenty-five years of experience. Crossen

* Abridgment of paper presented at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

stated that 88 cases have been reported in the world literature. He reported 1 additional case.

We can therefore estimate from available world literature that between 50 and 90 cases of carcinoma of Bartholin's glands have been reported, including recent reports from the foreign literature.[1,2,6,21,25,34] The number varies according to the rigidity of the criteria which one chooses to apply to the cases.

The normal embryology and histology of Bartholin's glands are perceptible in the female embryo of nine weeks. The glands appear as paired, solid, epithelial outgrowths from the vestibular epithelium of the urogenital sinus.[3,16,28]

In the female adult each gland measures 2 by 13 mm. The glands lie on the urogenital diaphragm in the paravaginal tissue, surrounded by the vascular vestibular bulb, being separated from the vagina by the bundles of the vaginal sphincter and part of the perineal soft tissues. The chief excretory duct lies within 1 to 2 mm. of the border of the labium minus, with its lumen opening into the vestibule just below the border of the hymen (1 cm. above the fourchet). The gland is well encapsulated. Cullen described the arrangement of the gland as follows: "The entire gland may be likened to a bunch of grapes, developed more on the one side than on the other. The main duct corresponds to the stem; the secondary and terminal ducts to the branches; and the lobules represent the individual grapes."

Bartholin's gland is a mucus-secreting gland of tubulo-alveolar character.[22] The normal histologic picture is unique and is not simulated by any other glandular structure of the labia.[4] The terminal excretory ducts are lined with one to several layers of cells that are cuboidal to columnar in charter, and unite into an ampulla lined by columnar epithelium. The true excretory duct is lined with flattened transitional or vestibular squamous epithelium.[28]

As with carcinoma in general, the etiology of carcinoma of Bartholin's glands is obscure. The role of chronic inflammation, previously thought of etiologic importance, is probably not noteworthy. More than half of the patients whose cases have been reported have been more than fifty years of age; the condition has been reported to have afflicted unmarried women, but never as yet a virgin.[13]

The early diagnosis of malignancy of Bartholin's glands is made probably less frequently than that of malignancy of any other organ of the body.[27] This would not be true if all "cysts or abscesses" of this gland were made the subject of careful pathologic study.[4]

Carcinoma of Bartholin's gland is first noted as a small, hard, painless, nodular swelling lying deep in the posterior portion of the labial fat, movable at first but months or years later becoming fixed to surrounding tissue. Then pain develops and commonly is referred to the coccyx or rectum. Because of the associated vulval edema, this pain is exaggerated by menstruation or coitus. After a variable interval, parts of the growth become necrotic and semifluctuant and, when overlying skin is destroyed, the tumor becomes infected, giving rise to a chronically discharging sinus. The malignancy tends to invade deeply to involve surrounding fat and muscle, and later the pubic bones. The inguinal lymph nodes are enlarged in more than 50 per cent of cases, either by metastatic involvement or secondary to vulval necrosis and infection.

Histopathologically, these tumors have features of architectural arrangement and cytologic detail in common with the epithelium of Bartholin's glands and ordinarily the growths can be recognized as having arisen from that gland.[27] Because of the two different kinds of epithelium found in Bartholin's glands, it is not surprising to find here two histopathologically different growths: adenocarcinoma (columnar) and squamous-cell carcinoma, both analogous to neoplasms of the uterine cervix.[27] Adeno-

carcinomatous types predominate over squamous-cell types in the proportion of 2.5 to 1.[28,31]

Rabson and Meeker quoted J. H. Honan (Ueber die Carcinome der Glandulae Bartholini, Inaugural Dissertation, Berlin, 1897) as enumerating four criteria before an indisputable diagnosis of primary carcinoma of Bartholin's gland can be made: (1) typical vulval site, (2) position deep in the labium, (3) connection with the duct of the gland and (4) presence of intact glandular tissue. If, in addition to the above, the skin is intact and the malignancy is adenocarcinomatous in type, the greater vestibular gland is unquestionably the primary site. However, it should be remembered, as noted by McDonald and others,[19,20] that vulval sweat glands can give origin to adenocarcinoma. Other adenomatous structures, which rarely present in the vulva, and which even more rarely become malignant, are accessory breast tissue and remnants of the wolffian duct system.

With respect to squamous-cell carcinoma, the problem of primary site is not readily clarified because the patient may neglect examination until the adjacent vulva is grossly involved, at which time the site of origin is lost. However, in early cases the point of origin can be more easily ascertained. If, on histopathologic study, normal glandular structure lined by columnar epithelium is seen contiguous to the squamous-cell malignant growth, it is assumed that the origin is the stratified squamous epithelium which normally lines the main excretory duct or that the normal columnar and transitional cells of the deeper portion of the duct system have undergone metaplasia to squamous cells, such as occurs in the presence of chronic infection of Bartholin's glands.[32]

In differential diagnosis, it is necessary to consider primary tuberculosis of Bartholin's glands, of which 3 cases have been reported, syphilis, which rarely attacks these glands, and sarcoma, which is extremely rare in this anatomic region.[35] Infection of Bartholin's glands, gonorrhea for instance, is usually bilateral and tends to regress with treatment.

In general, the prognosis of malignancy of Bartholin's glands is poor, the most important factor in the poor prognosis being failure to make early diagnosis. Boughton expressed the belief that malignancy here is curable if excision is done before the capsule has been invaded. In most reports of cases, the final outcome is not stated. Falls quoted Trotta (*Arch. di ost. e gin.*, 1900, p. 193) as reporting the only six-year cure up to the period of his (Falls') report. Lyle mentioned 3 cases of recurrent adenocarcinoma of Bartholin's gland (from Dr. W. P. Healy's files), in all of which operation previously had been performed for supposedly benign lesions, and in all of which the patients were well four or five years after the most recent operation. Rabson and Meeker, after communication with Mayo and Barber, and with Lyle, regarding survival of patients who previously had been the subject of report by these latter authors, stated that 2 patients were alive eleven years after the original operation. Rabson and Meeker also noted that the longest survival after surgical operation which had not been supplemented by radiotherapy was three and a half years. Simendinger stated that of 21 cases concerning which information on recurrence was available, there was no recurrence in 1 case after six years, in 1 case after four years, in 5 cases after two years, and in 4 cases after one year. Taussig noted that 3 patients with carcinoma of Bartholin's glands were alive five years after treatment. Hynes recorded that 1 patient was clinically well three and a half years after radical excision with cautery. LeDoux's patient who had a squamous-cell carcinoma, grade 3, of Bartholin's gland, had survived seven years, to the time of LeDoux's writing, with no recurrence, after radical excision and postoperative application of radium.

Lyle expressed the belief that malignant growths of Bartholin's glands should be

treated as vulval carcinoma; namely, by primary wide excision of the vulva, followed by secondary dissection of the inguinal and femoral lymph nodes. He gave as his opinion that local and regional irradiation are of value. Taussig's and Folsome's view agree with the one just expressed except that both of the latter expressed the belief that preoperative and postoperative irradiation are of no value.

Most authors have set down the belief that carcinoma of Bartholin's glands metastasizes by way of the lymphatic structures as does vulval carcinoma. Taussig described the lymphatic drainage from the vulva as passing chiefly through the inguinofemoral nodes of both sides, and less extensively through the external iliac, obturator, hypogastric and ureteral lymphatic chains. Since special study of the lymphatic drainage of Bartholin's glands has not been undertaken, Boughton expressed the belief that the application of conceptions of vulval lymphatic drainage in treatment of malignancy of Bartholin's glands is open to question, especially if the carcinoma under consideration is believed to have arisen in the deeper portions of a gland. It is interesting to note that Rabson and Meeker's patient, accidentally killed nine months after surgical operation and irradiation, was found to have extensive metastatic growths in the brain, dura, lungs, heart, liver and so on, with no evidence of local recurrence; such widespread metastasis suggests spread via the blood stream.

Cowper's glands (the bulbo-urethral glands) should be of collateral interest in this study. They are the male homologues of Bartholin's glands. The organic similarity of structure of the two sets of glands has been described by Schaffer. Cowper's glands are two small, round or oval structures lying in the urogenital floor, between the two layers of the median perineal aponeurosis, and between the deep surface of the membranous urethra, at the level of of the triangular ligament, and the apex of the prostate gland. They are of mucous, tubulo-alveolar structure and their alveoli are lined with low columnar cells; mucus-secreting elements are present in great numbers.[12] Only 6 cases of primary malignant tumor of Cowper's glands have been reported in the literature; all were adenocarcinomas with structure suggesting cylindroma. Chief complaints were of rectal pain, mass in the perineum and urinary disturbances. Treatment has been perineal cowperectomy followed by implantation of radon and use of roentgen therapy. Routine rectal examination is the most important method of arriving at a correct preoperative diagnosis.

REPORT OF CASES

CASE 1 (previously reported by Hunt and Powell and Mayo and Barber). This patient was married and had had 1 child. She was thirty-seven years of age when she registered September 26, 1924. Four years before, she had noted a cystic tumor in the vulva. The tumor had enlarged very slowly except for the past year, when, she thought, the rate of growth had increased. Examination revealed a nonulcerated, solid tumor in the region of the left Bartholin gland and enlarged right inguinal lymph nodes. At operation, September 30, 1924, the tumor was excised. The sphincter muscle of the anus was infiltrated and in all likelihood all of the tumor was not removed. The pathologist's report read: "Adenocarcinoma grade 2 of Bartholin's gland (5 by 4 cm.)."

Postoperative radium therapy was outlined October 31, 1924. The operative wound was healed. The inguinal nodes on the right were finely nodular and enlarged.

An American-type tube, the wall of which consisted of 0.5 mm. silver, and which contained 50 mg. of radium sulfate (element), was placed in a vaginal applicator. Filtration was through an additional 1 mm. of brass and 2 mm. of hard rubber. The outside diameter of the apparatus was 1.5 cm. and the length, 4 cm. One applicator was applied at a time to each of three fields: the operative site, the middle vaginal segment and the low vaginal segment. Each applicator remained in place for fourteen hours. The areas over the right and over the left inguinal lymph nodes, and the vulval area, were mapped out in small fields measuring about 4 by 4 cm. There was a total of six fields in each groin area and of four fields in the vulval area.

The applicator was a balsa wood block, of which the base measured 3 by 4 cm. and the thickness was 2.5 cm. To this block one American-type tube, of the sort previously described, was attached and filtration through an additional 2 mm. of lead and through an additional 2 mm. of rubber was provided. Three of these blocks were applied at a time, first to the right and next to the left groin. Some of the exposures were for fourteen and some for twenty hours. Two of these blocks were applied at a time to the vulval fields and were left in place for fourteen hours each.

The patient returned many times for reexamination. Naturally, the data that follow will be only a portion of the record.

She returned February 4, 1931, stating that for the past ten days a nodule had been present at the site of the old operation. Two days later the tumor and scar tissue were excised. The pathologist's report read: "Adenocarcinoma, grade 2."

Between February 11, 1931, and May 20, 1932, the patient received colloidal lead phosphate intravenously.

She returned April 26, 1933. At this time the scar tissue in the primary site was very firm and abundant. However, a small, oval infiltration in one of the heavy strands of scar tissue could be palpated. Punch biopsy was done. A pathologist's report read: "Adenocarcinoma, grade 1." There was a nodular infiltration measuring 1 by 1.5 cm., low in the pole of the right labium majus. Two platinum-iridium needles, each containing 1 mg. of radium sulfate (element) and the walls of which were 0.4 mm. thick, the diameter of each, 1.25 mm., and the total length of each, 10.0 mm., were placed in the substance of the oval infiltration and six needles were placed in the tumor that had been found in the labium majus; all of these eight needles were left in place for forty-eight hours.

The patient reported again January 15, 1934. At this time there was a small region of infiltration in the fourchet (right posterior). Biopsy resulted in a report of adenocarcinoma, grade 1. Nine of the needles previously described were placed in the region of involvement and were left there for forty-eight hours.

When the woman returned on September 11, 1934, there was definite subcutaneous infiltration, 1.5 cm. in diameter, in the left perineal region, near the anal wall. Punch biopsy was done and the pathologist's report read: "Adenocarcinoma, grade 1." Five of the needles previously described were placed in this region and were left in place for forty-eight hours.

At the patient's revisit, January 15, 1935, infiltration on the left side, very near the external urinary meatus, was found. Seventeen needles of the kind previously described were placed in this area and in the adjacent left labium majus, where they were left for twelve hours.

On August 18, 1936, the patient visited us again. The infiltration in the old treatment field, low in the right labium majus, seemed to have increased in size. There was a cutaneous infiltration near the anus on the right side, 0.5 cm. in diameter. Fifteen needles of the type previously described were distributed in these regions of activity and remained in place for forty-eight hours.

Again the woman returned, December 8, 1936. She complained of pain in the right hip and that this pain extended down the upper part of the right thigh. Roentgenograms of the right hip revealed metastasis to the neck and trochanteric region of the femur. Roentgen therapy was employed as follows: 200 kv., distance 50 cm., 15 ma., filtration 0.75 mm. copper and 1.0 mm. aluminum, time 30 minutes each to two large anterior and two large posterior fields in the region of the head of the femur. Subsequent examinations proved the treatment to have been effective.

On October 11, 1943, when the patient was seen again, extensive malignant activity was present in the primary field and in other vulval and perineal regions. Micturition and defecation were painful and difficult. The inguinal lymph nodes were bilaterally enlarged. The inguinal areas were mapped out in four small fields on each side and the small, balsa wood block applicators, previously described, were applied four at a time and were left in place for fourteen hours each. The vulval area and the perineal area were taken together and divided into two large fields, each about 7 cm. square. To each of these fields a balsa wood block which measured about 7 cm. square at the base and which was 5 cm. thick was applied. On the upper surface of each block were four American-type tubes, previously described, and filtration through an additional 2 mm. of lead was provided. The blocks were left in place, on one area at a time for twenty hours.

When the patient returned, January 20,

1944, she had only fair control of urine and feces. Activity included the vulval and perineal regions. The orifices of the vagina, urethra and anus could not be identified. Radium was applied by limited contact to selected fields of the above regions. Four American-type tubes, of the sort previously described, contained in rubber tubing of which the wall was 2 mm. thick, were strapped together with adhesive plaster, forming a surface applicator; application was for three and a half hours to each of six areas.

At the revisit of June 21, 1944, urinary distress, especially nocturia, urgency, frequency, and slight loss of control were the woman's chief complaints. There was definite activity in the old treatment fields. The pubic, vulval and anal areas were mapped out in four small fields each and four small block applicators, previously described, were applied, four at a time to each area but to only one area at a time, for twelve hours.

On September 29, 1944, when the patient returned again, she was hospitalized on account of vesical stones. The urethra was dilated easily to a size of 29 F. Two calculi were found in the bladder; litholapaxy was done and the fragments evacuated. The radium therapy carried out at the last previous visit was repeated.

On account of urinary retention, the woman returned April 15, 1945. Under general anesthesia, the scarred urethra was located and dilated to a size of 28 F. The bladder contained 2,000 cc. of urine. The vesical mucosa was markedly hemorrhagic. A No. 24 irrigating catheter was put in place.

The last admission of the patient to the hospital was September 23, 1946, for nursing care. The course was slowly retrogressive. On account of metastasis to the cervical portion of the spinal column, and to effect relief of pain, roentgen therapy was given December 30, 1946, using the following factors: 130 kv., distance 16 inches, 6 ma., filtration 5 mm. aluminum, time 17 minutes to each of four fields, two anterior and two posterior to the left shoulder. The same treatment factors were employed January 14, 1947, for further palliation.

Death occurred January 24, 1947. At necropsy the carcinoma was found to have extended to the liver, lungs, ribs, spinal column, cecum and so forth. Ulceration of the perineum, destruction of the anal sphincter, chronic cystitis, subacute ureteritis, pyelitis, bilateral pyonephrosis and hydronephrosis also were noted.

Comment on Case I. The patient survived twenty-six years after onset of the disease. At the time of the operation the primary lesion invaded the anal sphincter and was only partially excised. The inguinal lymph nodes were enlarged. Radium therapy in the beginning was designed for cure but later was applied in a limited way because palliation was all that could be expected. Roentgen therapy was given for control of skeletal metastasis, relief of pain and, in the main was only limited.

The treatment employed was effective; however, not sufficiently so to account for the many years of survival after the onset of the disease. It seems likely that, through the entire clinical course, carcinomatous activity was taking place, primarily or secondarily, in various regions. The denuded surface of the primary field was finely granular and waxy in appearance and did not bleed easily with slight trauma. The inguinal lymph nodes felt like shot, were discrete and were slow in growth. From the standpoint of the therapeutic radiologist, the explanation of the longevity is found in the growth characteristic of this malignant lesion. Further investigation may furnish the answer to the problem. The many unusual features present in this case prompted the idea to include mention of carcinoma of Cowper's glands in this report The few cases of this condition that have been reported may be relevant to the present study because, in most of them, the tumors were suggestive of cylindroma, as was the tumor in this case, according to at least one pathologist who reviewed the tissue.

CASE II (previously reported by Mayo and Barber). This patient was married and had had 2 children. She was forty-one years of age when she registered March 11, 1931. For at least two years the patient had known of a small lump in the left external genitalia.

Examination revealed a small, movable nodule in the left labium majus. The nodule was

widely excised and the pathologist's report read: "Adenocarcinoma (11 by 6 mm.) grade 1, of Bartholin's gland." The pathologist appended a note stating that he had not known this type of lesion of the labia to recur or metastasize.

Seven days later, prophylactic radium therapy was applied. The applicator was a small balsa wood block, previously described, and an American-type tube, the wall of which consisted of 0.5 mm. of silver and 1 mm. of brass, and which contained 92 mc. of radon. This apparatus was applied to the left labium majus for four hours.

In all reports, a good local result (primary field) was recorded. The last letter received was dated July 9, 1937.

Comment on Case II. The primary lesion was a growth of low grade of malignancy, probably encapsulated. It was widely excised and radium therapy was employed as a prophylactic procedure. The ultimate prognosis for this type of carcinoma is very good, however, when treatment is by surgery alone. The survival time from the onset of the disease to the last report was more than five years, probably seven or eight years. Further attempts at follow-up investigation have not been successful.

Case III (previously reported by Mayo and Barber). This patient was married but had had no children. She was fifty years of age when she registered June 26, 1933.

The patient reported having a lump in the vagina the size of a hen's egg. The onset, she said, was four years before and, during the interval, the lump had slowly enlarged. Six months before her registration, the patient had noticed a small lump in the right groin and recent swelling of the upper part of the right thigh.

Examination revealed a tumor in the situation of the right Bartholin gland and another tumor near the gland. Lymphedema affected the entire right leg and thigh and was graded 2 on a basis of grades 1 to 4, in which grade 1 indicates the least and grade 4 the greatest severity.

At operation, June 28, 1933, the small metastatic growth in the vicinity of the right Bartholin gland was excised with the gland. The pathologist's report read: "Nodule, vaginal wall, (3 by 2 cm.) squamous cell epithelioma grade 2." Postoperative radium therapy designed for palliation was begun July 5, 1933. The American-type tube, containing 48 mc. of radon, with additional lead filtration, was placed in two positions at the operative site and was kept in each position for eight hours.

The area of the right inguinal lymph nodes was mapped out in sixteen small fields. Sixteen small balsa wood blocks, were placed, four at a time, over these fields; the applications lasted for fourteen hours. Eight similar fields were treated in a similar manner in the area of the left inguinal lymph nodes.

The patient returned October 26, 1933. The condition at the operative site seemed satisfactory at that time but the lymphedema of the right leg persisted.

Roentgen therapy was given as follows: 200 kv., 50 cm. distance, 5 ma., 0.75 mm. copper and 1.0 mm. aluminum, time one hour and ten minutes to six large pelvic fields.

August 28, 1934, the patient reported by letter that the left leg had begun to swell five weeks previously.

The patient returned December 29, 1934, at which time lymphedema of both legs was present.

A letter was received from the attending physician February 27, 1935, reporting massive edema of both legs and of the left labium majus. However, the operative site was free of active malignant disease. The course of the disease was slowly and steadily retrogressive. Death was reported as having occurred September 1, 1936.

Comment on Case III. This patient had a vaginal tumor for four years before she sought treatment. Six months before institution of surgical treatment and limited radium therapy, metastasis to inguinal lymph nodes had taken place and, somewhat less time before institution of treatment, edema of the upper part of the right thigh had been noticed. Evidently, palliation was effected in that the primary lesion was controlled. The survival time from the onset of the disease was seven years.

Case IV. This patient was married and had had 4 children. She was seventy-one years of age when she registered December 11, 1933. The woman had found a small ulcer in the right

side of the vulva in April, 1932. The lesion had been curetted and treated by electric cauterization elsewhere. In July, 1933, the ulcer had recurred and, in November, 1933, the patient had found a tumor, the size of a hickory nut, in the right groin.

Examination at the Clinic revealed a region of infiltration, with ulceration, in the right labium majus and an enlarged right inguinal lymph node. The tumor of the right labium and region of Bartholin's gland and the enlarged lymph node of the right groin were removed surgically December 14, 1933. A rubber drainage tube was placed in the surgical wound of the right groin. Surgically, the lesion was considered to be a primary carcinoma of Bartholin's gland, metastasizing to the right inguinal lymph nodes. The pathologist's report read: "Squamous cell epithelioma grade 2 in both surgical specimens."

Radium therapy was applied twenty-four hours later. The American-type tube containing 50 mg. of radium sulfate (element) was introduced through the surgical drainage tube and was allowed to rest in two separate locations in the depth of the wound for fourteen hours in each location.

One vaginal applicator, cylindrically shaped, measuring about 5 cm. in length and 2.5 cm. in diameter, contained one American-type tube and additional filtration of 2 mm. of lead and 1 cm. of rubber was furnished; this device was placed in the vaginal cavity and was kept there for ten hours. Four American-type tubes in rubber tubing were strapped together to make a surface applicator. The apparatus was applied to the low angle of the surgical wound of the right vulva and was left in place for three and a half hours.

The patient revisited the Clinic, March 29, 1934. At this time her general condition was very poor on account of steady advance of the malignant disease and hemorrhage in the region of the metastatic growth in the right groin. The surgical site in the vagina and right side of the vulva seemed free of malignant activity.

The right inguinal region was mapped out in twenty-five fields and the small balsa block applicators were applied four at a time and were left in place for fourteen hours, until all fields had been covered. The same region was mapped out in three large fields and the large block applicator was applied to each field and was allowed to remain in place for twenty hours.

The patient returned May 2, 1934. Much palliation had occurred in that the malignant activity in the fields of treatment was reduced.

Two American-type tubes were placed in a shallow sinus in the right groin. The total radon content was 55 mc. and the duration of treatment was twelve hours. The inguinal region was mapped out in twelve small fields to which the small balsa wood blocks were applied four at a time and were left in place for fourteen hours each.

Death occurred July 16, 1934.

Comment on Case IV. The course in this case was modified by treatment given elsewhere. The primary lesion had metastasized to the inguinal lymph nodes at the time that radium therapy was applied. The treatment was designed for palliation only. The malignant process was locally arrested. Survival time from the onset of the disease was two years.

CASE V. This patient was married but had had no children. She was forty-seven years of age when she registered December 29, 1934. For eight months she had noticed a painless swelling, the size of a walnut, in the left portion of the vulva, posteriorly. The tumor had been widely excised elsewhere September, 1934, but a pathologist's report was not available. The woman noted soreness in the perineum December 12, 1934, and a definite tumor, December 23, 1934.

Examination at the Clinic revealed a firm infiltration in the posterior lateral wall of the vagina at the introitus, beneath the skin of the perineum and near the anterior rectal wall. Inguinal adenopathy was not found.

The clinical diagnosis was carcinoma of Bartholin's gland, modified by surgery. A piece of tissue was removed from the wall of an ulcer which composed a portion of the partially necrotic, infiltrated tissue of the vaginal wall. The pathologist's report read: "Squamous cell epithelioma, grade 4."

On December 31, 1934, seventeen platinum-iridium points were placed in the tumor field and were left in place for forty-eight hours. Sacral block anesthesia was used. A few days later the vaginal applicator was placed, first in the middle, and then in the lower segment of the vagina and was left in these fields for fourteen and ten hours respectively. The American-type tube contained in a lead cylinder the wall of which was 2.0 mm. thick, all enclosed in a

finger cot, was placed in the depth of the crater-like ulcer in the vagina, where it was left for fourteen hours. The large block applicator was placed, first in the pubic and then in the vulval field for twenty hours each. Six small balsa wood block applicators were applied to treatment fields over the right and the left inguinal lymph nodes as a prophylactic procedure. Three blocks were applied at a time, on one side at a time, until all fields had been covered. Each field was exposed for fourteen hours.

The patient revisited the Clinic February 15, 1935. The ulcer in the vagina seemed healed. There was a small draining abscess (localized) in the left part of the perineum. Radium therapy was not applied at this visit.

The woman returned May 18, 1935. Her general health was very good. She was actively employed. A minimal, stellate scar replaced the ulcer of the vagina and vulva. There was a nodular infiltration about 1 cm. in diameter in the lower pole of the left labium majus. Nine platinum-iridium points were placed in this region of infiltration and were left in place for forty-eight hours. The large vaginal applicator was placed in the low vaginal segment and was left there for eight hours. Eight small balsa wood block applicators were applied in the regions of the right and of the left inguinal lymph nodes. Four of these were applied at a time, on one side at a time, until all fields had been covered. Following each application the applicators were left in place for fourteen hours.

The patient revisited the Clinic again October 23, 1935. She was in excellent general health. Minimal scars replaced infiltrated tissue. No active malignant infiltrations were made out. However, there was an indefinite, enlarged node in the right inguinal region. Eight small balsa wood blocks, previously described, were applied, four at a time, for fourteen hours each to the region of this enlarged node.

In a letter dated May 22, 1948, the patient was reported to be in excellent health and actively engaged in her own merchandise establishment.

Comment on Case V. Progress in this case was modified by surgical operation performed elsewhere, before the patient came to the Clinic. The lesion was of a high grade of malignancy. The radium therapy applied was designed for cure. The result obtained, as determined from the date of onset of the disease and the date of the last report, may be classed as, at the least, a fourteen year "cure."

Case VI. This patient was single and was fifty-three years of age when she registered June 27, 1935. She had found a lump between the vagina and rectum about June 1, 1935. She always had been of delicate health. Menopause had been brought on by roentgen therapy in 1929 because of menorrhagia. A nervous breakdown also was recorded in her history.

Examination revealed two tender nodules, one in the left paravaginal region and the other in the left pararectal region, infiltrating the inferior pole of the left labium majus. One mass was slightly fixed. One small, palpable, right inguinal lymph node was found. On proctoscopic examination, the following were found: a mass, measuring 3 by 6 cm., lying anterior to and to the left of the anus and lower part of the rectum, extending down to the external anal margin and adherent to the rectal and anal wall at the level of the anterior crypts. Bimanual pelvic examination and minimal laboratory determinations gave essentially negative results.

At operation, July 1, 1935, a nodule in the region of the left Bartholin gland or its duct was removed for biopsy. Several hard nodules extending into the rectovaginal septum were found. The pathologist's report read: "Tissue from region of left Bartholin's gland, squamous cell epithelioma grade 4."

Radium therapy as a palliative procedure was begun July 8, 1935. Two large, cylindrical vaginal applicators were placed one at a time, first in the deep and then in the middle vaginal segment. Treatment in each of these fields was for fourteen continuous hours. A rectal dilator containing three American-type tubes, containing a total of 133 mc. of radon equally distributed and filtered through an additional 1.0 mm. of brass and about 1.0 cm. of wood which composed the wall of the dilator, was placed in the anus and held firmly against the anal region for three hours. A large balsa wood block applicator was placed over the vulval area and was kept there for twenty hours. Roentgen therapy, 200 kv, 50 cm. distance, 10 ma., copper 0.75 mm. and aluminum 1.0 mm., time 28 minutes, was applied to each of four large pelvic fields; this was started on July 12, 1935 as daily treatments.

The patient revisited the Clinic October 28, 1935. Following the treatment she had tired easily, had been very weak and a distressing

diarrhea had lasted for several weeks. Her convalescence had been slow; however, her bowels were functioning regularly by the time of her return to the Clinic, her appetite was good and she had gained 4 pounds (1.8 kg.).

The mass in the lower pole of the left labium majus was considered to measure 3 by 4 cm. and to be movable. Further radium therapy was outlined. The large vaginal applicator was placed longitudinally, deep in the vaginal cavity and was left in place for fourteen hours. The rectal dilator was similarly placed and remained in position for two and a half hours. Seventeen platinum-iridium needles were placed in the infiltrated tissue of the perineal body, where they remained for forty-eight hours. Pus excaped through a puncture wound. It was enlarged and an iodoform wick was introduced. At this time the anal mucosa was ulcerated.

The patient revisited the Clinic February 25, 1936. Her general condition was slightly improved; however, she was uncomfortable on account of the perineal involvement. The size of the perineal tumor had remained about stationary; nevertheless, there was an increase in the extent of the infiltration into the rectovaginal wall. There was a small sinus, patent to gas, connecting the lower part of the rectum and the perineum in the tumor field.

Further radium therapy was outlined. The large vaginal applicator was applied, first in the deep and then in the middle vaginal segments; it remained in place for six hours in each location. Two American-type tubes containing a total of 113 mc. of radon, were placed in the sinus that has been described, where they were left for eight hours. Two similar tubes, containing 74 mc. of radon, were placed in the region of ulceration in the tumor field, where they remained for four and a half hours. Five gold radon seeds (wall 0.3 mm.), containing a total of 4 mc. of radon, were distributed in the infiltrated tissue of the rectovaginal septum.

Death was reported as of September 29, 1938, by letter, evidently caused by progression of the malignant disease.

Comment on Case VI. The rather superficial expression of the disease was favorably influenced by cautious radiation therapy, since palliation was all that could be expected. The malignant lesions were multiple when first seen and were considered inoperable. The time of survival was three years from the onset of the disease.

Case VII. This patient was married but had had no children. She was thirty-one years of age when she registered September 2, 1940. A left perineal tumor had been present for one year. About six times, a hemorrhagic, purulent material had been discharged from the mass and, each time, healing had followed. The tumor had been removed in the patient's home city in July, 1940. A slide of tissue from the tumor was sent to the Clinic where the pathologist who examined it reported: "Squamous cell epithelioma grade 2 (Bartholin gland)."

Examination revealed a large, recurring growth in the left side of the vagina. The inguinal lymph nodes were bilaterally enlarged. Minimal laboratory determinations gave essentially negative results.

At operation, September 5, 1940, the tumor was surgically removed. It had penetrated deeply near the pubic bone. The wound was left open for postoperative radium therapy. All tissue bearing lymph nodes in the inguinal and saphenous regions, and in the inguinal canal up to the level of the internal ring, was dissected out.

The pathologist's report read: "Vulva, squamous cell epithelioma grade 2. Lymph nodes, right side, metastatic squamous cell epithelioma grade 2. Left side, inflammatory tissue."

Twelve days after the operation that has been described, radium therapy was started. Two American-type tubes of monel metal, the walls of which were 1.5 mm. thick, containing 50 mg. of radium sulfate (element), were placed each in a lead jacket the wall of which was 2.0 mm. thick. The foregoing packets were placed singly in the distal and in the proximal portions of the vaginal wound. Each application was of ten hours' duration. The areas of the right and left inguinal lymph nodes were mapped out, each area in ten small fields, to which the small balsa wood block applicators were applied, about four at a time on the right and four at a time on the left, until all areas had been treated.

The patient returned January 7, 1941. The malignant process was active in the vagina and probably in the region of the inguinal lymph nodes.

A specimen then was removed from the anterior left wall of the vagina. The infiltrated tissue was cauterized. The pathologist's report read: "Squamous cell epithelioma grade 2."

Three days following the above procedure, contact radium therapy was outlined for the

vaginal fields. Three American-type tubes, packaged as previously described for a surface applicator, provided from 80 to 90 mc. hours of radiation per square centimeter for each application until all the surface of the area of involvement had been covered. In this case, six applications that varied from three to four hours each were required. The inguinal areas again were treated with the small balsa wood block applicators, as previously described.

The patient returned again May 9, 1941. Much palliation had been effected. Tissue change due to treatment was present in the vagina. No treatment was outlined at this visit.

On August 4, 1941, the woman returned again. The tissue change due to treatment had subsided. One application, for contact surface treatment, was made to an area of activity in the vagina (3 tubes for three hours). The inguinal lymph nodes seemed inactive.

When the patient returned on January 19, 1943, there was a crater in the left perineal area and in its deep portion was a urinary and fecal fistula. The anal area seemed intact. Edema of the left thigh and leg was graded 2. Bimanual rectal palpation revealed fixation and infiltration, graded 3 in extent, in the left adnexal tissues. The patient was actively employed. No treatment was recommended.

In the last letter received, dated January 3, 1944, the patient was reported to be bedfast.

Comment on Case VII. Progress in this case was modified by surgical operation performed before the patient came to the Clinic. We found an extensive vaginal carcinoma, with metastasis to the inguinal nodes. The vaginal growth was excised and the inguinal lymph nodes of both sides were dissected out. Postoperative radium therapy was limited in amount and the palliation secured was limited. Survival time from the onset of the disease was four years and four months to the time of the most recent report.

SUMMARY

The first patient of those whose cases have been reported was treated in 1924, and the last, in 1940. Some of the applicators used early in this experience are not employed today. The technique of radium therapy during the past twenty-four years has been definitely improved.

There were 7 patients in the group. All were married except 1 but, of those who were married, half had not had children. The youngest patient was thirty years of age and the oldest patient was sixty-nine years of age at the onset of the disease. The average age at registration was 47.1 years.

Two patients had had the condition for about four years, 2 patients for approximately two years, and 1 for one year before they came to the Clinic. The remaining 2 patients reckoned their illness in terms of months up to the time when we first saw them.

On admission, conditions were as follows: In Case II the primary lesion was clinically localized. The primary lesion in Case I had invaded the anal sphincter muscle and the inguinal nodes were enlarged. In Case III multiple tumors were present in the region of Bartholin's gland and inguinal lymph nodes were clinically involved. The primary lesion was ulcerated in Case IV and metastasis to the inguinal lymph nodes had taken place. The patient in Case V presented a large, recurring, ulcerated tumor but no definite inguinal adenopathy. In Case VI were multiple lesions in the primary field, adherent to the anal and rectal wall with involvement of inguinal nodes. A large, recurring tumor, with metastasis to the inguinal lymph nodes, was present in Case VII.

All primary lesions were studied microscopically. Five lesions are reported to be squamous-cell epitheliomas and 2, adenocarcinomas. The adenocarcinomas were of low grade of malignancy; 1 was of grade 1 and the other of grade 2. The squamous-cell epitheliomas also favored the low grades; 3 were of grade 2 and 2 were of grade 4. When all lesions are considered, 5 were of low grade and 2 of high grade of malignancy.

In 5 cases the primary lesion was surgically excised at the Clinic. In 1 of these 5 the excision was partial. Of the 2 remaining cases, in 1 wide excision had been performed before we saw the patient and no excision was performed at the Clinic. In the remain-

ing case of the 2, tissue was removed only for biopsy.

All patients received radium therapy. In 1 case radium was used prophylactically. A complete course of radium therapy designed for cure was given in 1 case. In 1 case radium therapy which originally was intended for cure was later limited to use for palliation. Four patients received limited radium therapy, designed for palliation throughout. Three of the 7 patients received supplemental roentgen therapy.

The primary lesion in only 2 cases was considered localized while in the remaining cases there was local dissemination or metastasis to the inguinal lymph nodes.

Four patients are known to have died of the disease, 1 patient was bedfast in 1944, 1 was living and seemed well in 1948, and 1 could not be followed after 1937. The longest survival from the onset of the disease was in Case I, in which the lesion was considered an adenocarcinoma, grade 2; the patient survived twenty-six years after onset of the disease. The second longest survival time after onset of the disease was in Case V, in which the diagnosis was squamous-cell epithelioma, grade 4. The woman was in good health fourteen years after the onset of the disease. Next in order of duration of life after onset of the disease was the patient of Case II, whose lesion was diagnosed adenocarcinoma grade 1. At the time when this report was written she was lost to our follow-up system; however, she was known to be in good health seven or eight years after onset of the disease. In Case III, in which the diagnosis was squamous-cell epithelioma grade 2, the survival time was seven years after onset of the disease. In Cases VII and VI, in the former of which the diagnosis was squamous-cell epithelioma grade 2 and, in the latter, squamous-cell epithelioma grade 4 the patients were known to have lived, respectively, more than four years and three years after the onset of the disease. The shortest survival time after onset of the disease was two years, occurring in Case IV, in which the diagnosis was squamous-cell epithelioma grade 2.

CONCLUSIONS

1. Carcinoma of Bartholin's glands (greater vestibular glands) is rare and the carcinomas tend to be of low grade of malignancy.

2. Carcinoma confined to a Bartholin gland, of low grade of malignancy, if wide excision is followed by prophylactic radium therapy, should not recur.

3. Clinically extensive carcinoma of a Bartholin gland, localized to the primary field, if treated with radium designed for cure, regardless of grade, may not recur.

4. Surgery, radium therapy and roentgen therapy in combination constitute effective methods for control of carcinoma of Bartholin's glands.

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EFFECTS OF REPEATED LOW DOSES OF NEUTRONS ON THE ESTROUS CYCLE OF THE WHITE RAT*

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IN THE course of investigating the general effects of repeated low doses of neutrons on white rats, it was noted that doses of 1.8 n given six days a week for seven to nine months caused a reduction in the growth rate but no change in the picture of the peripheral blood.[5] Among the small number of animals, a large percentage of those given the low doses and 2 animals given twelve daily doses of 10 n each developed tumors of the breast, kidney and lymphoid tissue.

In continuing these investigations, the first phase undertaken was a study of the estrous cycle of the white rat by the vaginal smear method of Long and Evans[6] to determine whether the cycle was affected by neutron irradiation. Bischoff *et al.*[1] irradiated six week old mice with single doses of 200 and 400 r of roentgen rays. At the 200 r level, irradiation markedly reduced the frequency of estrus, increased its frequency during the fourth month, followed by a six month period during which estrus did not differ significantly from that of the controls. With a dose of 400 r, estrus in the mice was abolished following irradiation and the frequency of estrus established for the controls was not attained throughout a thirteen month period. Drips and Ford[2] found, on irradiating a group of rats with 1/10 to 1/15 the human erythema dose of roentgen rays, some temporary irregularities in the estrous cycle. Skipping of one or two cycles and prolongation of the cornified stage were the principal variations observed. Slight congestion of the ovaries in those animals killed within a few days after irradiation was the only pathological change.

The above data indicate that some effects of neutrons on the estrous cycle of the rat are to be expected. Furthermore, in light of the recent publication of Gates and Warren[4] on the vaginal smear as a diagnostic aid in the early detection of uterine cancer in humans, it was thought that the appearance of tumors induced by neutron irradiation might be reflected in the estrous cycle of the rat.

EXPERIMENTAL PROCEDURE AND RESULTS

Forty-six female white rats, varying in age from forty-two to sixty-six days, were taken from fourteen litters raised in the colony of the Biochemical Research Foundation, and were divided into two groups of 23 each. One group constituted the experimental animals to be irradiated and the other served as the non-irradiated control. All time data are given in terms of the number of days after the date the two groups were established.

Beginning with the twenty-fifth day of observation, when the rats were from sixty-seven to ninety-one days old, daily vaginal smears were made on all animals according to the method of Long and Evans[6] to establish the normal picture of the cycle. Smears were then made almost daily until the 176th day of observation when the rats were 218 to 242 days old. Irradiation of the experimental group began on the fifty-second day and continued until the ninety-fourth day at which time irradiation was discontinued. Vaginal smears showed that the non-irradiated group exhibited normal and regular cycles of from four to six days' duration. In contrast, the irradiated group showed disruption of the pattern of the cycle during and following the period of irradiation (Fig. 1) with finally the reappearance of a normal cycle. No abnormal cells were observed in any of the vaginal smears.

The animals were irradiated by the cyclotron of the Biochemical Research Foundation under the direction of Dr. Theodore Enns according to the procedure described previously by Enns *et al.*[3] A daily dose of 3 n was given in approxi-

* From the Biochemical Research Foundation, Newark, Delaware.

mately seven minutes, six days a week, until the total dose of 111 n (37 doses in a total of 42 days) had been administered. This was the only feature in which the treatment of the irradiated groups differed from that of the controls.

At intervals during the investigation, the animals were weighed and these results, in terms of the average for each of the two groups, are given in Figure 2. Hematological studies indicated that the only observable changes brought about by the neutron irradiation was a lowering of the white blood cell count to a minimum of 6,000 to 7,000 per cu. mm. after sixteen doses of neutrons, followed by recovery.

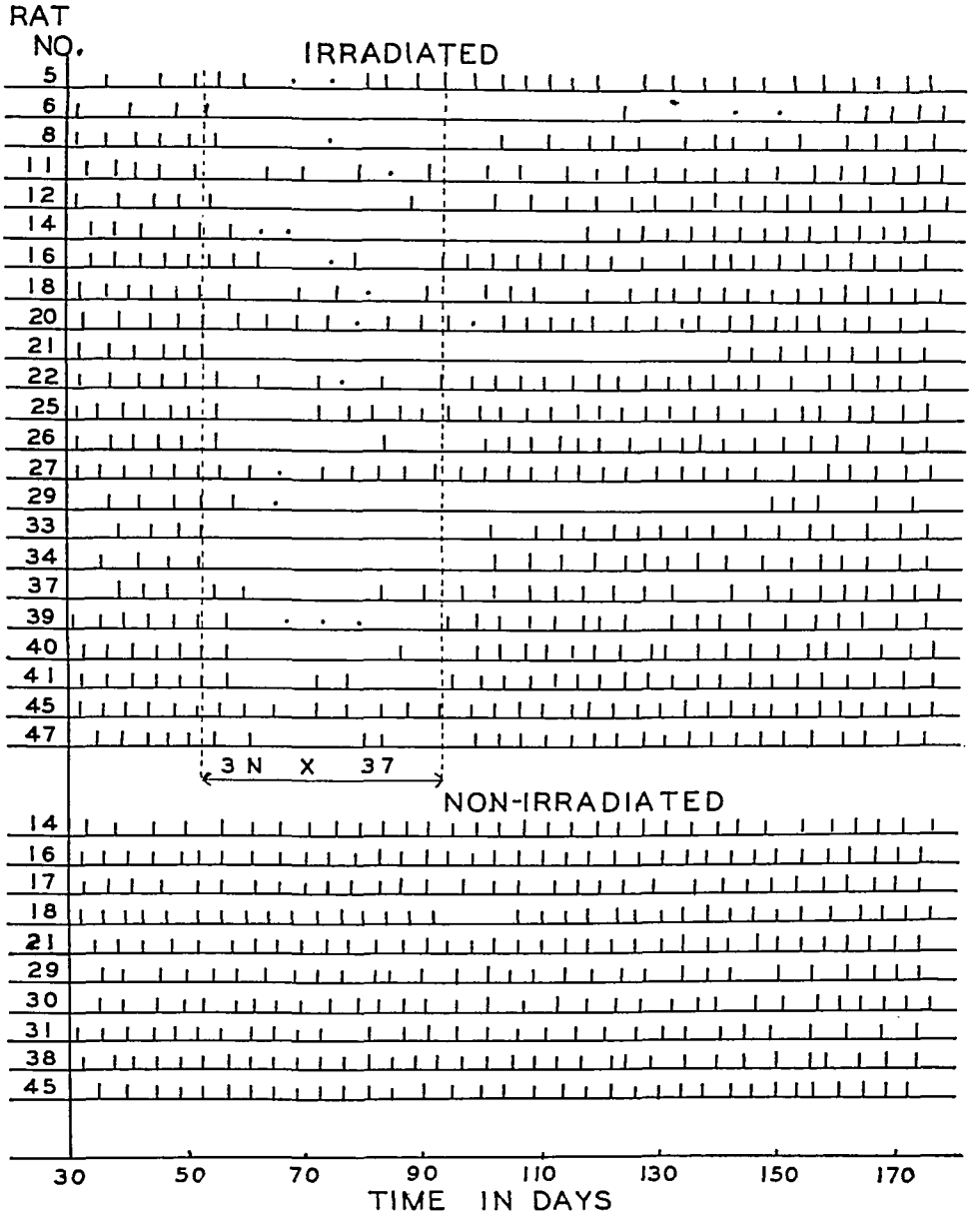


Fig. 1. Frequency of the estrous cycle in the irradiated and in some of the non-irradiated rats. The vertical line indicates the time of appearance of the so-called "cheesy-cornified" stage (stage 3 of Long and Evans). A dot indicates an abnormal cycle.

Discussion

The estrous cycles of all irradiated rats and of a representative number of the non-irradiated are represented diagrammatically in Figure 1. In these figures, the vertical line indicates the conspicuous so-called

"cheesy-cornified" stage of a normal cycle, which is stage 3 of Long and Evans.[6] In some instances, especially during the period of irradiation, the "cheesy-cornified" stage was not apparent although there occurred occasionally a stage showing some cornified cells but always mixed with some epithelial cells, a condition designated in Figure 1 by a dot.

The radiation level of 3 n per day was very satisfactory for demonstrating the effect of neutrons on the estrous cycle. From Figure 1 it can be seen that a wide range of effects on the cycle was produced. In rats 6, 8, 21, 29, 33, and 34, the normal cycle was completely inhibited during the period of irradiation and for a varying length of time afterwards. The maximum effect was shown by rats 21 and 29 which did not show a return to a normal cycle for forty-six to fifty-five days, respectively, after termination of irradiation. In contrast to the above reaction, only a slight irregularity in the estrous cycle was observed for rats 5, 20, 22, 27, and 45. The other rats of the irradiated group showed changes in the cycle varying widely between these extremes.

None of these rats showed a prolonged or continuous or increased frequency of estrus during the period of observation, as was found in mice following roentgen-ray doses of 200 and 400 r by Bischoff *et al.*[1]

None of the irradiated rats could be considered ill during the period of observation although they all showed a low white blood cell count together with an initial loss of weight. As is shown in Figure 2, following a slight loss in weight, growth was resumed but at a rate somewhat below that of the corresponding controls. In this connection it is interesting that thirty-seven doses of 3 n each had a more profound effect on the rats than the 172 or 251 doses of 1.8 n each, reported previously by Leitch.[5] In the latter experiments, a reduced growth rate was the only effect of the irradiation, there being no initial weight loss and no hematological effects. From these two series of experiments it would appear that the daily doses of 1.8 and 3 n lie in a very critical range that requires further investigation.

Neutron irradiation affects the estrous cycle of the white rat even when low doses are used. However, considerable more data

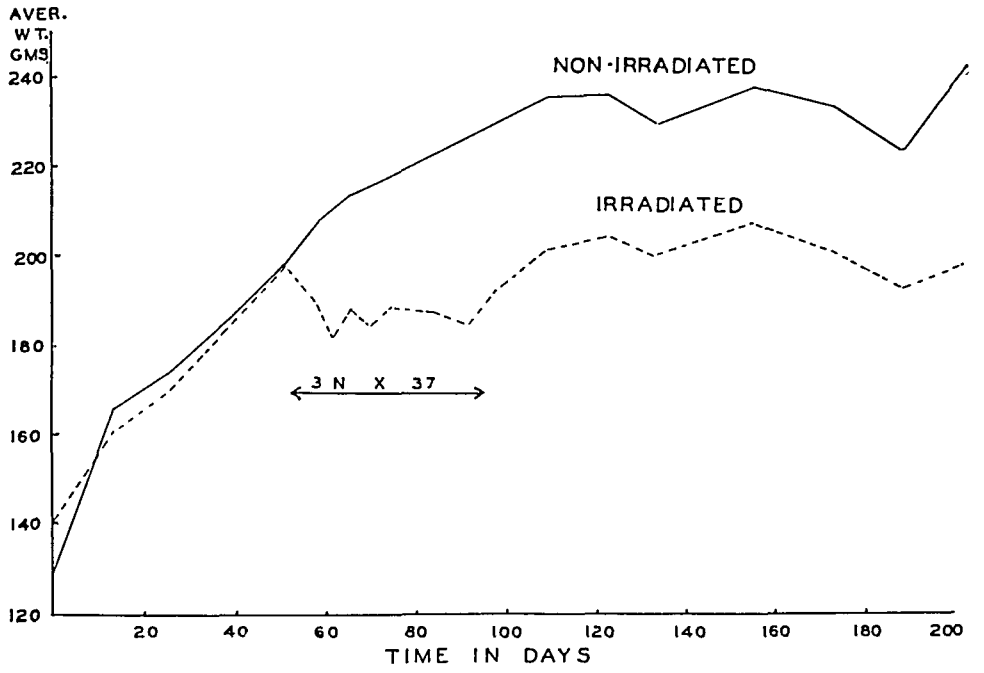


FIG. 2. Average weights of the irradiated and the non-irradiated rats during the period of investigation.

dealing with the effects of varying neutron doses given during different time intervals are required before the full relationship between neutron dose and effects on the estrous cycle can be worked out. Furthermore no conclusions can be drawn at this time concerning the mechanism of this action.

Since the animals used in this experiment are still being observed for the induction of tumors, no data can be reported at the present time on either gross or microscopical pathology. It can be reported now that rats 5, 18, 26, and 27 have already developed tumor-like swellings in the mammary region. Reference to Figure 1 indicates that these 4 rats showed no unusual changes in the estrous cycle as a result of irradiation.

SUMMARY

Neutron bombardment of twenty-three rats at the rate of 3 n daily for thirty-seven exposures caused a disruption of the estrous cycle as indicated by vaginal smears, a retardation of growth and temporary reduction in white blood cells in the circulating blood.

Swellings appeared in the mammary region of four rats uncorrelated with estrous cycle variations.

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PHARMACOLOGICAL REACTIONS OF SERA AND DRUGS IRRADIATED WITH ROENTGEN RAYS OF VARYING WAVELENGTH*

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PHYTOTOXICITY

TWENTY-FIVE years ago, one of the authors, being interested in some of the general laws of pharmacology, began a study of the relative sensitivity of animal and vegetable protoplasm to various drugs and chemicals.[1] This marked the beginning of a new department of biology to which the name of *phytopharmacology* was given. It was soon discovered that living plant-physiological test objects were much more sensitive to certain poisons than animal tissues are and, vice versa, other poisons were much more toxic for living animal protoplasm than for vegetable protoplasm. As a result of these experiments, it could be generally stated that poisons or toxins derived from animals are much more poisonous for vegetable protoplasm than for animal protoplasm and, vice versa, most of the poisons derived from the plant world are usually much more poisonous for living animals than for living plants. This general observation was particularly true of toxins present in the blood of human beings. By means of phytopharmacological tests it was definitely demonstrated that there were poisonous substances or toxins present in certain pathological conditions which could not be demonstrated by zoological experiments nor by ordinary chemical methods.

The effects of drugs and poisons on plants can be studied in many ways. These methods have been described elsewhere.[2] For convenience and for quantitative determination, it was found that the growth or elongation of the straight single roots of *Lupinus albus* seedlings grown in plant physiological solutions under standardized ecological conditions were most suitable for practical medical purposes. As published elsewhere,[3] it was shown that normal blood sera dissolved in 1 per cent solutions of Shive[4] medium caused but little inhibition in the root growth of lupine seedlings. The phytotoxic index or ratio of growth in a 1 per cent serum solution compared with controls grown in plant physiological saline solution ranges from 70 to 75 per cent, and this is true for blood sera of all animals, both warm-blooded and cold-blooded, with the exception of reptiles.[5] In the case of human blood serum, a number of pathological conditions were found to yield much more toxic effects and have lower indices of growth. This was true of the following conditions: catamenia or menstruation, pernicious anemia, trachoma, leprosy, and especially the very grave skin disease known as pemphigus. Each of these diseases yields a characteristic phytotoxic effect, and these blood sera can be differentiated from each other by various other properties, particularly by their responses to ultraviolet radiations.

RADIATION AND PHARMACOLOGICAL STUDIES

Even twenty years ago when the phytotoxic properties of pernicious anemia were first discovered by Macht, it was found that exposure of such blood sera in quartz containers to an ultraviolet mercury vapor lamp for a few minutes was followed by a complete detoxification of the serum as indicated by phytopharmacological assay.[6] Macht and Anderson went further and

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† Dr. Ostro died on May 12, 1948.

found that therapeutic irradiation of patients suffering from pernicious anemia produced a diminution in toxicity or even complete detoxification of their blood, concurrently with improvement in their blood morphology and clinical improvement of the patients' general health. Curiously enough, however, when similar irradiation experiments were tried in quartz containers on blood sera from leprosy and trachoma and on menstrual serum, no detoxification occurred. Neither was there any detoxification produced by such ultraviolet irradiation in the blood of pemphigus.[7]

In the last three years, the authors have been engaged in a study at the Sinai Hospital of Baltimore, of the effects of roentgen rays on various properties of the blood and on the pharmacological properties of a number of drugs. For this purpose, a Westinghouse roentgen therapy machine was employed with and without filters. It was found in the experiments on blood that when normal serum is exposed to roentgen rays filtered through a composite filter of 1 mm. Al and 2 mm. Cu, or through a filter of 1 mm. Al and 0.5 mm. Cu, its phytotoxic properties were either unchanged or usually made more toxic. On the other hand, when the blood serum of patients afflicted with pemphigus was treated with roentgen rays filtered through a composite filter, its characteristic toxic properties were destroyed. This occurred in so many experiments that the irradiation method is now employed in this laboratory as a confirmatory test for the diagnosis of pemphigus.[8] Briefly stated, an ordinary phytopharmacological examination of pemphigus serum gives a *toxic* index of growth but when the same serum is treated with filtered roentgen rays the *toxicity disappears*. The two tests together establish a positive diagnosis of pemphigus because no other skin disease gives the same reactions. The factors employed in the irradiation are 200 kv., 20 ma., and target distance of 50 cm.

The present authors, furthermore, found that the toxicity of the blood in true pernicious anemia is also rapidly destroyed by the above roentgen rays, filtered through a composite filter. On the other hand, catamenial blood serum, the serum of trachoma and leprosy blood were not detoxified by such rays when tested by phytopharmacological methods.

Two other blood conditions yielded interesting results in connection with irradiation studies. The authors found that the blood serum of hemophiliacs can be made to clot more quickly by short (but not prolonged) exposures to specially filtered roentgen rays.[9,10] Again, more recently, studies have been made by one of the authors on the phytopharmacological properties of bloods from all kinds of mental diseases, and it was found that all true psychoses yield blood sera which are toxic for plants and the toxicity can be measured quantitatively by phytopharmacological methods. These blood sera from cases of psychoses are very quickly detoxified when treated with small doses (60 to 100 roentgens) of roentgen rays filtered through a composite filter.

The laboratory observation in vitro in regard to the detoxification of pemphigus serum by roentgen irradiation warranted a trial of roentgen therapy in 2 patients dying with pemphigus vulgaris. The idea was to endeavor to produce detoxification of the pemphigus poison by small doses of deeply penetrating roentgen rays. These patients were given short radiation over the hepatic and splenic regions. The results were amazing. The patients' blood was detoxified, as indicated by pharmacological tests described above, and the clinical condition of the patients was improved. Both of these patients are alive and in good health at the writing of this paper, three years after the beginning of the disease,* and this is itself a remarkable record for the usually fatal disease, pemphigus vulgaris.[11] Since the initiation of these radiotherapeutic studies, a series of other patients was given similar treatment, and more or less improvement was noted in 75 per cent of them. These

*Also in March, 1949.

are described elsewhere. [12] Here again the factors used were 200 kv., with 20 ma. and target distance of 50 cm.

EFFECTS OF DIFFERENT FILTERS

Perhaps the most interesting observations made by the authors from the standpoint of biophysics was the undoubted fact, as far as biological reactions are concerned, that the detoxification of pemphigus serum both in vitro and in vivo was produced best only when short roentgen rays were employed, obtained by filtration through a composite filter of 1 mm. Al and 2 mm. Cu. Thus, for instance, when pemphigus blood serum was treated in vitro with these rays in doses of 100 r, complete detoxification occurred. On the other hand, however, when another sample of the same original serum was treated with exactly the same dosage, 100 r, using 0.5 mm. Cu filter, very little or no detoxification occurred. Apparently there was a qualitative difference in the biological effect of the rays taking place, which is contrary to the usual teachings of physicists.

In order to clarify as much as possible this puzzling observation, the aid of a well known physicist was enlisted for further research on the problem. Dr. Scott W. Smith, x-ray physicist at the National Bureau of Standards, Washington, D.C., was invited to calibrate the roentgen apparatus employed for therapy at the Sinai Hospital, Baltimore, and to aid in constructing a physical apparatus by which roentgen rays differing widely in their quality range could be employed for pharmacological research. This was done by Dr. Smith as follows: Five different sets of filters were selected, their absorption curves and half-layer values were determined and different voltages were selected which would yield exactly the same intensity or dosage of roentgen rays and yet furnish aggregates of roentgen rays definitely different in quality. Table 1 gives the physical data which we obtained in our biophysics experiments. For briefness, the five filters are designated as A, B, C, D, E. Starting with this apparatus, we exposed specimens of various kinds of pathological blood sera as well as a number of drugs, and after exposing them to exactly the same dosages of the roentgen rays, experiments were made to ascertain if any differences in the pharmacological

TABLE I

PHYSICAL FACTORS FOR THERAPY CONE 15 BY 15 CM.

Symbol	Kv. (peak)	Ma.	Filter	r/min.	Time for 100 r
A	200	20	0.93 mm. Cu	24.0	4 min. 10 sec.
B	160	20	0.62 mm. Cu	13.5	7 min. 24 sec.
C	126	20	0.31 mm. Cu	8.2	12 min. 12 sec.
D	100	20	6.25 mm. Al	3.4	29 min. 24 sec.
E	80	20	4.16 mm. Al	1.35	74 min. 0 sec.

TABLE II

PHYSICAL FACTORS FOR THERAPY CONE 6 BY 8 CM.

Symbol	Kv. (peak)	Ma.	Filter	Half-Value Layer	r/min.	Time for 100 r	Effective Wave-length
A	200	20	0.93 mm. Cu	1.03 mm. Cu	20.70	4 min. 50 sec.	0.17 Å
B	160	20	0.62 mm. Cu	0.67 mm. Cu	11.70	8 min. 34 sec.	0.19 Å
C	126	20	0.31 mm. Cu	0.28 mm. Cu	7.10	7 min. 6 sec.	0.27 Å
D	100	20	6.25 mm. Al	4.10 mm. Al	2.94	34 min. 0 sec.	0.39 Å
E	80	20	4.16 mm. Al	3.00 mm. Al	1.17	85 min. 30 sec.	0.52 Å

properties could be detected. As will be seen, the results established conclusively that there were marked differences in the pharmacological effects produced by the rays filtered through different filters.

Table I shows the physical data established for the roentgen apparatus employing a therapy cone of 15 by 15 cm. Table II gives the factors which we employ more frequently with a therapy cone 6 by 8 cm. for irradiating sera and drugs in small open top glass containers at a distance of 50 cm.

IRRADIATION OF BLOOD SERA

The changes produced in sera and drugs by irradiating them with roentgen rays, employing various filters, administered in exactly the same dosages were studied in some cases by zoopharmacological methods, in other cases by phytopharmacological methods, and in still other cases by biochemical tests. The results obtained are here briefly presented. The blood sera studied came from the following pathological conditions: catamenia, trachoma, leprosy, pemphigus, pernicious anemia, and psychoses. It was found that menstrual serum and the sera of leprosy and trachoma irradiated with roentgen rays passing through various filters did *not change* the phytotoxicity of these bloods as studied on seedlings of *Lupinus albus*. This is shown in Tables III and IV. On the other hand, the blood sera from all kinds of psychoses and from pemphigus were markedly affected by irradiating them with *some qualities* of roentgen rays and not affected by other qualities. This is strikingly illustrated by Tables V and VI, both of which are composite tables summarizing the results obtained in a large number of experiments. Thus, for instance, it will be seen that pemphigus serum is markedly detoxified when a composite filter of 1 mm. Al and 2 mm. Cu is used, whereas the same serum treated with roentgen rays passed through a filter of 0.5 mm. Cu was only slightly detoxified. Of the five individual filters, A, B, C, D, E, the most striking effect was obtained with Filter A which produced

TABLE III

RESISTANT BLOOD SERA

Leprosy Serum				Catamenia Serum			
Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index	Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index
Untreated control 1% solution	—	—	52%	Untreated control 1% solution	—	—	48%
Using Filter A	5 min.	100 r	49%	Using Filter A	5 min.	100 r	46%
Using Filter B	9 min.	100 r	52%	Using Filter B	9 min.	100 r	44%
Using Filter C	14 min.	100 r	56%	Using Filter C	14 min.	100 r	48%
Using Filter D	34 min.	100 r	50%	Using Filter D	34 min.	100 r	49%

TABLE IV

TRACHOMA BLOOD SERUM

Irradiated through Composite Filters of 1.0 mm. Al plus 2.0 mm. Cu			
Specimen No. 1	Phytotoxic Index	Specimen No. 4	Phytotoxic Index
Before irradiation	65%	Before irradiation	57%
After 110 r	57%	After 110 r	57%
Specimen No. 2		Specimen No. 5	
Before irradiation	55%	Before irradiation	55%
After 110 r	53%	After 110 r	47%
Specimen No. 3		Specimen No. 6	
Before irradiation	58%	Before irradiation	59%
After 110 r	61%	After 110 r	57%

TABLE V

PSYCHOTIC BLOOD SERA
(POOLED SPECIMENS)

Schizophrenic Sera				Manic Depressive Sera			
Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index	Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index
Untreated specimen	—	—	57%	Untreated specimen	—	—	50%
Using Filter A	5 min.	100 r	79%	Using Filter A	5 min.	100 r	71%
Using Filter B	9 min.	100 r	68%	Using Filter B	9 min.	100 r	62%
Using Filter C	14 min.	100 r	61%	Using Filter C	14 min.	100 r	54%
Using Filter D	34 min.	100 r	57%	Using Filter D	34 min.	100 r	50%
Using Filter E	85 min.	100 r	54%				

TABLE VI

PEMPHIGUS SERUM (POOLED SPECIMENS)

Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index of Growth
Untreated specimen	—	—	42%
Using Filter 0.5 mm. Cu	4 min.	100 r	52%
Using Filter 2.0 mm. Cu	6 min.	100 r	76%
Using Filter A	5 min.	100 r	73%
Using Filter B	9 min.	100 r	57%
Using Filter C	14 min.	100 r	46%
Using Filter D	34 min.	100 r	40%
Using Filter E	85 min.	100 r	35%

marked detoxification. Filter B produced slight detoxification while Filters C and D produced no effect and Filter E actually rendered the serum more phytotoxic. Very similar results were obtained with irradiating blood from psychotic patients. Blood sera from patients with pernicious anemia were also found to be detoxified by roentgen rays passed through a composite filter (Table VII).

Another interesting series of experiments was carried out with the blood of a patient suffering from hemophilia. This particular patient hospitalized in the wards of Sinai Hospital usually exhibited a very marked prolongation of his clotting time. Specimens of his blood were taken from an arm vein and the influence of roentgen rays of various wavelengths on clotting time was studied, as shown in Table VIII. Here it will be noted that the unirradiated serum took four hours forty minutes to clot whereas the normal clotting time in humans studied by the Lee-White method varies from five to ten and not more than fifteen minutes. When the whole blood from this hemophilia patient treated with roentgen rays passed through Filter A the clot-

TABLE VII

PERNICIOUS ANEMIA SERUM
(POOLED SPECIMENS)

Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index
Untreated control 1% solution	—	—	42%
Using filter of 1.0 mm. Al plus 2.0 mm. Cu	2 min.	36 r	56%
Using filter of 1.0 mm. Al plus 2.0 mm. Cu	4 min.	72 r	59%
Using filter of 1.0 mm. Al plus 2.0 mm. Cu	6 min.	108 r	67%
Using filter of 1.0 mm. Al plus 2.0 mm. Cu	8 min.	144 r	72%

ting time was cut down to one hour three minutes. Irradiation through Filter B prolonged the clotting time to one hour thirty-one minutes, whereas irradiation through Filter D prolonged it to two hours three minutes (Table VIII). In this case there was definitely a marked difference produced by equivalent dosages of roentgen rays but of different qualities. However, as has already been stated by the authors in an article on hemophilia, increasing the dosage beyond certain limits may *reverse* the thromboplastic effect of the roentgen rays.

TABLE VIII

HEMOPHILIA PATIENT
Nov. 12, 1947

Specimen	Clotting Time of Whole Blood
Untreated Serum	4 hr. 40 min.
Irradiated with 100 r Filter A	1 hr. 3 min.
Irradiated with 100 r Filter B	1 hr. 31 min.
Irradiated with 100 r Filter D	2 hr. 3 min.

IRRADIATION OF DRUGS

In addition to studies on blood we examined the effects of roentgen irradiation in vitro, using various filters, on the following drugs: tincture of digitalis, digitoxin, the venom of *Crotalus atrox* (rattlesnake), the neurotoxin of *Naja tripudians* (cobra venom), solutions of penicillin, both crystalline and amorphous, and streptomycin. The action of various qualities of roentgen rays on tincture of digitalis was studied in a large number of experiments by phytopharmacological methods,[13] on the one hand, and by intraperitoneal injections in white mice.[14] Tables IX and X reveal again the difference in the effects produced when different filters are used. This is especially well illustrated by the phytopharmacological assay which is a composite table of thirteen experiments using all five filters. It will be seen that irradiation through Filters A and B produces a marked decrease in the toxicity of digitalis for *Lupinus* seedlings.

TABLE IX

PHYTOPHARMACOLOGICAL ASSAY OF DIGITALIS TINCTURE. COMPOSITE TABLE OF 13 EXPERIMENTS WITH 1 PER CENT SOLUTION

Method of Roentgen Treatment	Duration	Dosage	Phyto toxic Index of Growth
Untreated specimen	—	—	51%
Using Filter A	5 min.	100 r	73%
Using Filter B	9 min.	100 r	72%
Using Filter C	14 min.	100 r	62%
Using Filter D	34 min.	100 r	58%
Using Filter E	85 min.	100 r	57%

Irradiation through Filter C produces only a slight effect while irradiation through Filters D and E produces still less effect. The protocols shown in Table X illustrate the results obtained with digitalis injections in mice. Here again it will be noted that irradiation through Filter A reduces the potency of digitalis much more than irradiation through Filter C, as indicated by the mortality of animals obtained in the experiments.

The effects of roentgen rays of various qualities on the most active principle of digitalis, namely digitoxin,* was studied by a chemical method, as well as on plants. The effects of irradiation of digitoxin in

TABLE X

DIGITALIS EXPERIMENTS ON MICE
OCT. 29–NOV. 7, 1947
Dosage 4 mg. per gram weight

I. Normal Tr. digitalis	4 mg. per gm. wt. Mortality 100% Phytotoxic index 51%
II. Irradiated through Filter A, 300 r	4.5 mg. per gm. wt. Mortality 25% Phytotoxic index 72%
III. Irradiated through Filter C, 300 r	4.5 mg. per gm. wt. Mortality 35% Phytotoxic index 62%

* The digitoxin was obtained from the Winthrop Company through the courtesy of their research director, Dr. Maurice Tainter.

TABLE XI

INFLUENCE OF ROENTGEN IRRADIATION ON DIGITOXIN (WINTHROP)
METHOD OF ANDERSON AND CHEN
Colorimetric Readings with Klett-Summerson Photoelectric Colorimeter

Concentration of Solution	Roentgen Treatment	Dosage	Phytotoxic Index	Colorimeter Reading
1:20,000 in alcohol	Not irradiated	—	74%	70.0
1:20,000 in alcohol	Using Filter A	200 r	50%	66.5
1:20,000 in alcohol	Using Filter B	200 r	48%	62.0
1:20,000 in alcohol	Using Filter C	200 r	46%	56.0
1:20,000 in alcohol	Using Filter D	200 r	44%	52.0

TABLE XII

COBRA VENOM (*Naja tripudians*)
COMPOSITE TABLE
SOLUTION IN PHYSIOLOGICAL SALINE 1:100,000

Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index of Growth
Untreated specimen	—	—	75%
Using Filter A	5 min.	100 r	82%
Using Filter B	9 min.	100 r	86%
Using Filter C	14 min.	100 r	90%
Using Filter D	34 min.	100 r	93%

alcoholic solutions were compared colorimetrically by the method of Anderson and Chen.[15] Table XI shows a definite difference produced by irradiation through the different filters (Table XI).

The effects of cobra venom were studied on both plants and animals. Assays of the solutions of cobra venom irradiated by different qualities of roentgen rays were made by the method of Macht on white mice.[16,17] It will be noted from Table XII that roentgen irradiation of cobra venom produces a deterioration or attenuation of the venom, but here again there was a difference in the degree of deterioration of the venom irradiated using Filters A and B, on the one hand, and of the venom irradiated using Filters C and D, on the other. Similar differences in toxicity of cobra venom were noted in phytopharmacological experiments on *Lupinus albus* seedlings[18] and here also a parallel difference in degree of decomposition was found in regard to roentgen rays filtered by different filters (Table XIII). The

TABLE XIII

ASSAY OF COBRA NEUROTOXIN ON BASIS OF 1 MOUSE UNIT PER 20 GM. MOUSE

I. Unirradiated solution	Mortality 90%
II. Irradiated 100 r through Filter A	Mortality 50%
III. Irradiated 100 r through Filter C	Mortality 30%

TABLE XIV

VENOM OF *Crotalus atrox* SOLUTION 1:5000
COMPOSITE TABLE

Method of Roentgen Treatment	Duration	Dosage	Phytotoxic Index of Growth
Untreated specimen	—	—	52%
Using Filter A	5 min.	100 r	64%
Using Filter B	9 min.	100 r	67%
Using Filter C	14 min.	100 r	79%
Using Filter D	34 min.	100 r	82%

venom of the rattlesnake was studied on the growth of plants as well as in regard to its toxicity for mice (Table XIV). The results obtained also definitely indicated a difference in pharmacological reaction produced in samples of the same venom solution treated with roentgen rays of different qualities.

In regard to the very important class of antibiotics, penicillin and streptomycin,

the pharmacological reactions were studied by phytopharmacological methods, on the one hand, and by biochemical methods, on the other. These studies are still in progress but it can be definitely stated here that a marked difference in pharmacological properties of both drugs was found between samples treated with roentgen rays passed through a composite filter of 2 mm. Cu and those treated with roentgen rays passed through a filter of 0.5 mm. Cu. Full data will be published in a separate paper.

Among the biochemical tests employed in studying penicillin as well as some of the blood sera were experiments concerned with oxidation-reduction phenomena. The Thunberg method was employed.[19,20] These studies are still in progress but it may be stated here that there was a definite difference noted after treatment of specimens of the sera and antibiotics, with roentgen rays passed through different filters. A very striking illustration is shown in Table xv which gives the results obtained with a specimen of pooled pemphigus serum both in regard to its phytotoxic index of of growth for *Lupinus albus* roots and the time required for decolorization of methylene blue by Thunberg's method.

Table XV

OXIDATION-REDUCTION EXPERIMENT (THUNBERG'S METHOD)
EMULSION OF WATER-SOAKED *Lupinus albus* SEEDS

Serum Examined	Roentgen Treatment	Phytotoxic Index	Time Required for Decolorization of Methylene Blue
Normal human serum	Untreated	75%	50 min.
Pooled pemphigus serum	Untreated	42%	2 hr. 0 min.
Pooled pemphigus serum	100 r through filter of 1 mm. Al plus 2 mm. Cu	80%	68 min.
Pooled pemphigus serum	100 r through filter of 1 mm. Al plus 0.5 mm. Cu	54%	1 hr. 45 min.

COMMENTS

While the above investigation is still in progress certain tentative conclusions are warranted on the basis of the numerous radiation and pharmacological experiments performed by the authors.

In the first place, roentgen rays produce marked changes in the pharmacological properties of some kinds of sera, and few or none on sera from other pathological conditions.

In the second place, similar changes in the potency of certain drugs are produced by irradiation with roentgen rays, some drugs developing a greater toxicity, and others revealing a diminished physiologic potency.

In the third place, in view of the quantitative pharmacological assays and the carefully controlled irradiation experiments with different filters and equivalent doses of roentgen rays, there is no doubt that roentgen rays of different wavelength produce changes in blood sera and in a number of drugs or poisons which are qualitatively and quantitatively different pharmacologically. What the ultimate explanation of the phenomenon may be is not yet certain; however, it is certain that treatment of blood sera and drugs with roentgen rays of different wavelengths is of considerable diagnostic value in medical work and may be of therapeutic importance, as has already been established by our experiences with pemphigus and hemophilia. The present research, although it must still be re-

garded as of a preliminary and heuristic nature, certainly warrants further investigation along the above most interesting lines.

Finally it must be emphasized that the above experiments with roentgen rays were all carried on in the laboratory (with two exceptions) and at present cannot be applied clinically without further work. The two exceptions are the diseases pemphigus and hemophilia concerning which some favorable therapeutic results in patients have already been obtained.

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THIMBLE CHAMBER CALIBRATION ON SOFT ROENTGEN RAYS

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I. INTRODUCTION

THIMBLE chambers of the Victoreen type are normally designed for the measurement of relatively hard radiations and are customarily calibrated using roentgen-ray beams which are produced by tubes with an applied voltage of 70 to 200 kv., and which are subjected to some preliminary filtration; at least 2 mm. of alumimum or 0.2 mm. of copper. Over this range, the chambers yield readings which are practically independent of the radiation quality when calibrated against a free-air chamber. However, in the absence of any other ionization chamber, they are frequently used for measuring very much softer radiations than those for which they are designed or calibrated. Numerous cases have come to our attention where the red bakelite 25 r chamber has been employed to measure radiations produced by potentials as low as 20 or 30 kv., and it has been obvious in many cases that the users have had no reasonable idea as to the magnitude of the errors* involved. It therefore appeared to be desirable to investigate the magnitude of these errors and provide some quantitative data thereon.

Measurements cited in this paper with respect to the effect of added filtration on the calibration relate primarily to one 25 r chamber. The effect of thimble chamber type is studied using red bakelite 25 r, 100 r, and 250 r chambers, as well as the newly designed 250 r nylon chamber. When calibrations are made in a given roentgen-ray beam, or in different beams of exactly the same quality, then, as noted below, different chambers of the same type generally require the same corrections.† Similarly, chambers of different types require different corrections.

While our results may be taken as typical, the very magnitude of the corrections required indicates that whenever a thimble chamber is to be used for precise measurement in the very soft roentgen-ray region, it should be specifically calibrated for the exact conditions under which it will be used. This becomes the more important, the lower the roentgen-ray excitation potential. The wave form of the excitation potential becomes increasingly more important at the lower potentials also.

It is desirable for thimble chamber readings to bear a constant relationship to those of a standard free-air chamber over a wide range of roentgen-ray quality. To achieve this, it is necessary that the type of absorption and scattering in the thimble chamber wall be equivalent to that which is observed in air, and, that the absorption in the wall thickness be negligible in comparison with the transmission through it, or, that the secondary corpuscular radiation within the cavity be enhanced by means of a suitable internal coating of the wall to compensate for radiation lost by absorption in the wall thickness.

The practical attainment of this requirement is not difficult for 50 to 200 kv. roentgen rays emitted by a tube whose inherent filtration is at least 0.2 mm. of copper. For example, in the measurement of radiation from such a tube, the Victoreen 25 r thimble chamber, with its 0.6 mm. red bakelite wall, reads only 5 per cent low for 50 kv. radiation if it reads correctly for 100 to 200 kv. radiation.

The problem is much more difficult, how-

* By "error" is meant the departure of r-meter readings from those of a standard free-air chamber.

† "Correction," as here used, is a factor by which r-meter readings must be multiplied to make them agree with those of a standard free-air chamber.

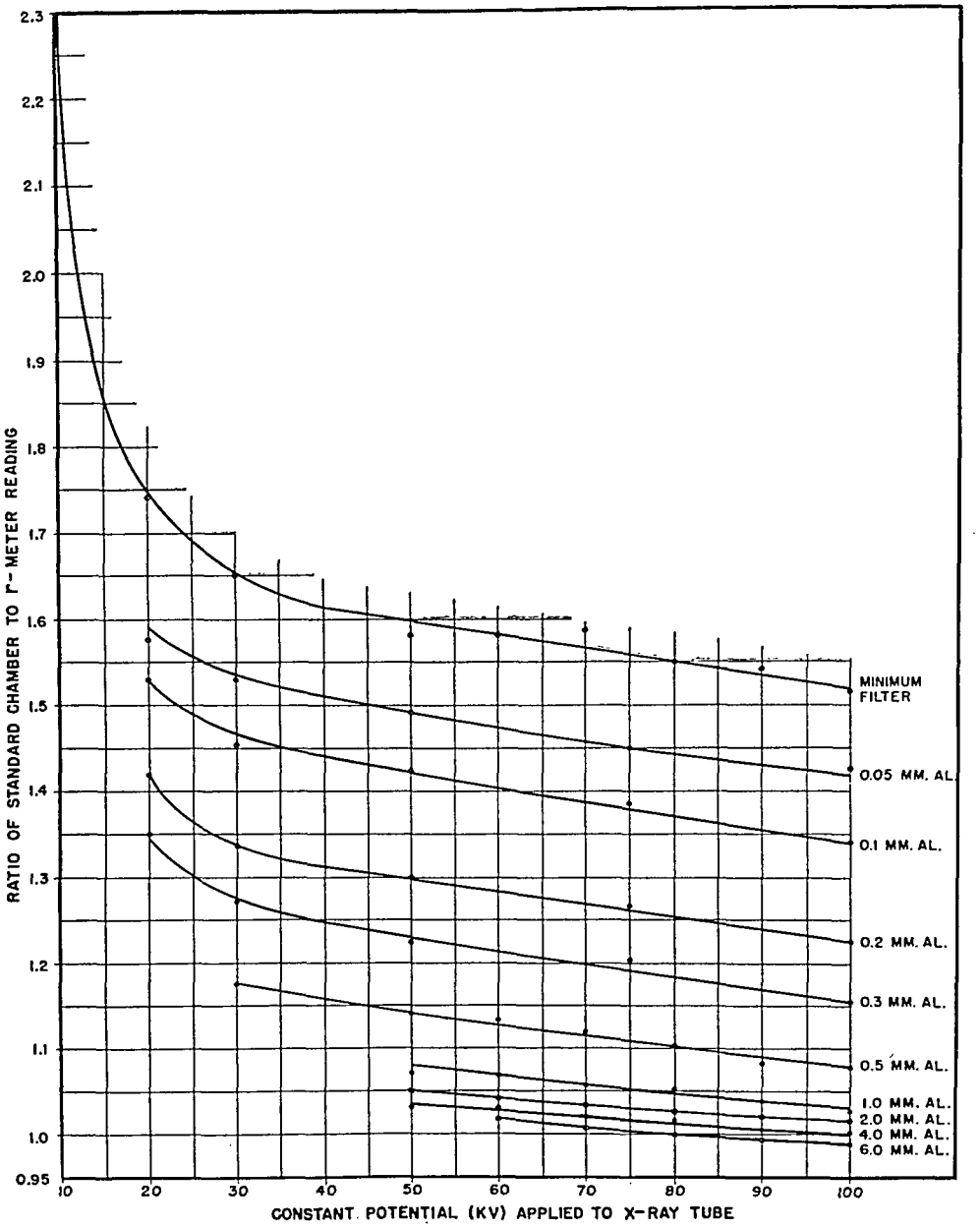


FIG. 1. The effect of roentgen-ray excitation potential and added aluminum filtration upon corrections required to the readings of a 25 r bakelite thimble chamber on r-meter No. 1193 when calibrated on roentgen rays generated by a tube with 1.5 mm. of beryllium inherent filtration.

ever, in the case of long wavelength roentgen rays, produced by a tube whose inherent filtration is, say, 1.5 mm. of beryllium. Roentgen rays as long as 4 Ångströms in wavelength are available in measurable quantity from such a tube, and these are readily absorbed, even in a few centimeters of air. There are applications where it is necessary to determine the exposure at or near the portal of a beryllium window tube. A properly designed chamber, therefore, should measure 4 Ångström roentgen rays (approximately 3 kv. quality), with a minimum of correction.

An attempt has been made in this direction,[1] utilizing an ionization chamber having a beryllium wall. The use of an open-air chamber has been reported,[2] utilizing a limiting diaphragm and a mesh type electrode system consisting of silk threads soaked in india ink to make them electrically conducting. A similar chamber has also been constructed,[3] substituting, in place of the mesh of silk threads, Kodapak

I, which is cellulose acetate sheet 0.00088 inch thick containing some plasticizer. Its calibration at the National Bureau of Standards yields scale factors (roentgens per scale division) which vary by less than 8 per cent as the roentgen-ray excitation potential is varied from 7.5 to 90 kv. and stances, 100 cm. of air at approximately 760 mm. of Hg pressure and 22° centigrade. It is necessarily a part of the minimum filtration, although it is not hereinafter so designated.

The standard ionization chamber used in in this comparison was the one designed for

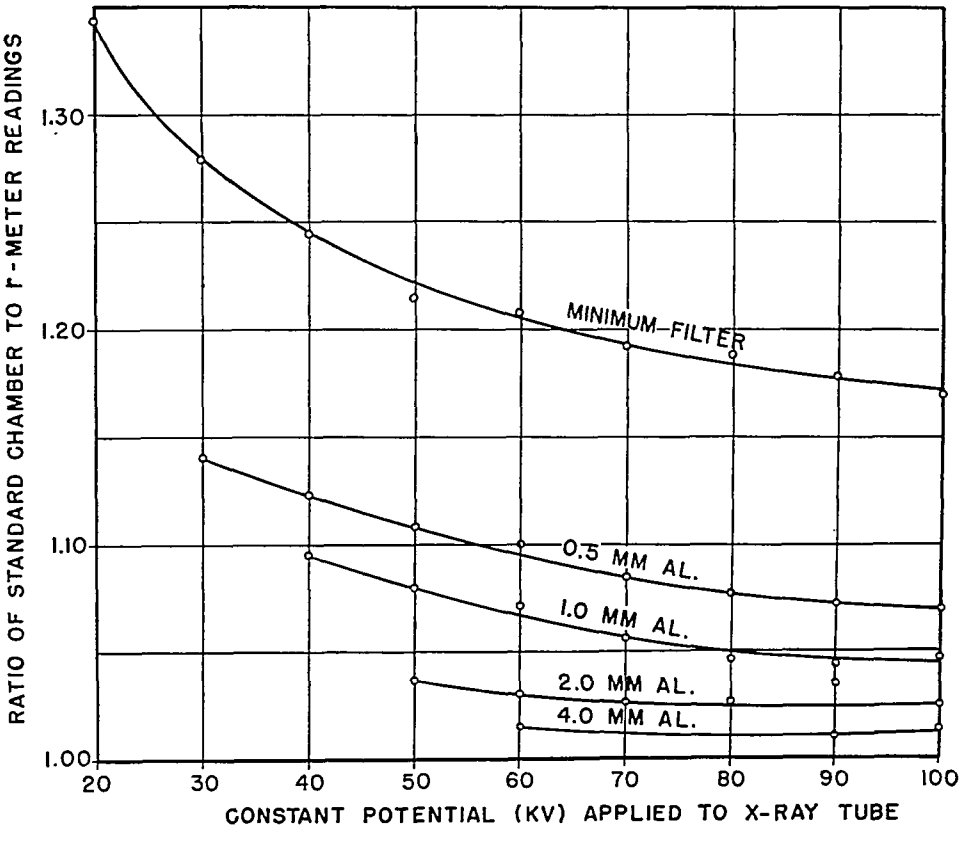


Fig. 2. The effect of roentgen-ray excitation potential and added aluminum filtration upon corrections required to the readings of a 25 r bakelite thimble chamber on r-meter No. 1193 when calibrated on roentgen rays generated by a tube with 1.3 mm. of cerium glass inherent filtration.

the filtration from the minimum of 1.5 mm. of beryllium plus 100 cm. of air to this plus 4 mm. of alumimum.

II. Experimental Procedure and Results

In this study, the usual substitution method was employed in the calibration of the thimble chambers, the radiation being first measured with a standard guarded field, free-air ionization chamber and then with the thimble chambers placed in the position of the limiting diaphragm. The filtration between the roentgen-ray tube portal and the ionization chamber is, in all in- measuring radiations produced by potentials up to 200 kv. It has an air path of 21.1 cm. between the limiting diaphragm and the front edge of the collector plate.[4] Corrections required for the air absorption over this distance vary from about 0.5 per cent for 200 kv. radiation to 33 per cent for 10 kv. radiation[5] and these have been applied in this calibration.

"Constant"* potentials varied in steps between 10 and 200 kv. were employed on each of two tungsten target roentgen-ray

* The power supply has a resistance-capacitance filter to reduce the ripple to 0.05 per cent per milliampere current drain, and currents used in these calibrations did not exceed 10 milliamperes.

tubes used in the calibration. The first was a thin-walled (1.3 mm.) cerium-glass tube, which offers about as little inherent filtration as any glass-window tube. The second was a 200 kv. water-cooled tube whose window thickness is only 1.5 mm. of beryllium, and which has almost no inherent filtration.

The r-meter readings were observed over approximately the same scale range to avoid any possible scale factor error, and were readily reproduced within ± 1 per cent. This is an over-all error, which includes fluctuations in the calibrating equipment of not greater than ±0.3 per cent.

Figure 1 shows thimble chamber corrections using the beryllium-window tube over the range of 10 to 100 kv., and for filtrations ranging from the minimum of 1.5 mm. of beryllium to this plus 6 mm. of aluminum of added filtration. For example, it is observed for the minimum filtration that the correction is 1.52 at 100 kv. and increases to 2.3 at 10 kv. It is obvious that with such a large correction, the calibration of a thimble chamber for use with very soft radiations must be made with considerable care. In fact some earlier studies[6] indicate the necessity of effecting a special calibration for each specific tube in conjunction with its own specific potential source. The addition of as little as 1 mm. of aluminum to the beam, however, reduces the error from 52 to 3 per cent at 100 kv. and from 60 to 8 per cent at 50 kv.

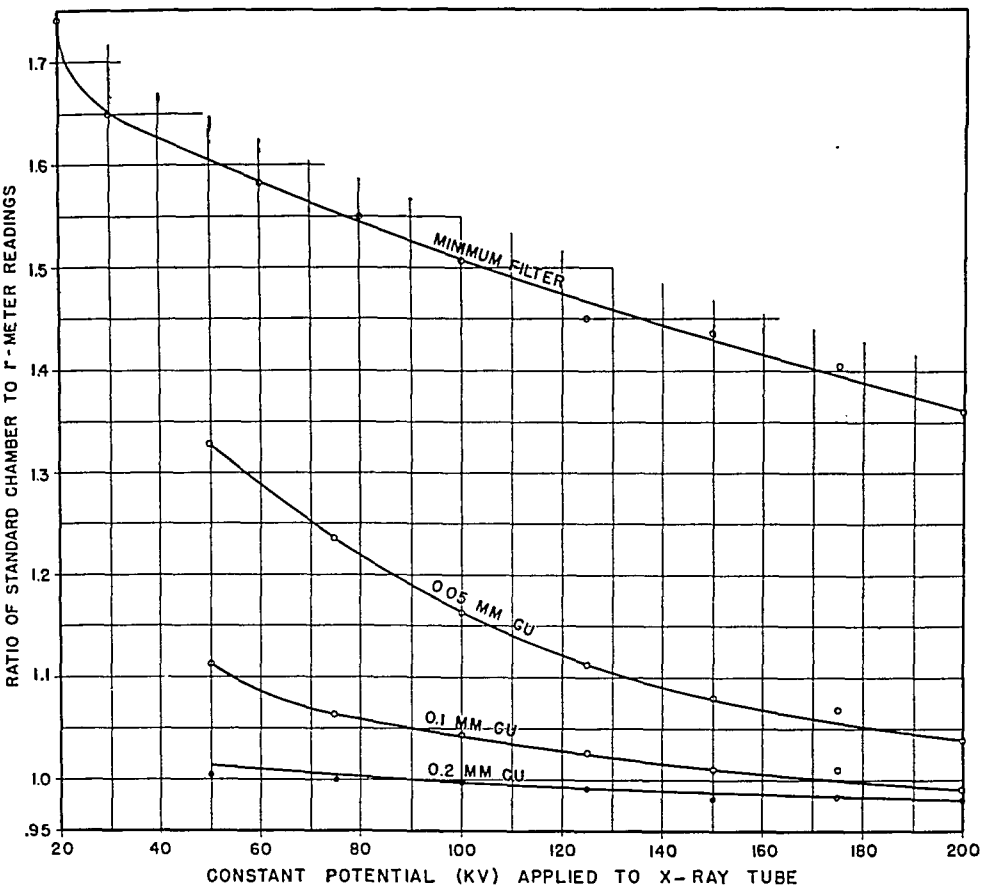


FIG. 3. The effect of roentgen-ray excitation potential and added copper filtration upon corrections required to the readings of a 25 r bakelite thimble chamber on r-meter No. 1193 when calibrated on roentgen rays generated by a tube with 1.5 mm. of beryllium inherent filtration.

Similar corrections using the 1.3 mm. glass-wall tube are shown in Figure 2. Here, for minimum filtration, it is seen that the correction varies from 1.17 at 100 kv. to 1.34 at 20 kv. Comparing these correc-

tions with those of the 0.3 mm. aluminum curve in Figure 1, it is found that they are closely alike over the whole potential range, indicating that the 1.3 mm. of cerium glass is equivalent in absorption to approximately 0.3 mm. of aluminum.

Calibration curves for the beryllium-window tube and copper filtrations at potentials up to 200 kv. are shown in Figure 3. It is observed that until approximately 0.22 mm. of copper filtration is added to the beam, the errors at low potentials are relatively large, 11 per cent, for example, at 50 kv. and 0.11 mm. of copper filtration. However, for 0.22 mm. of copper filtration, the thimble chamber agrees with the standard within ±2 per cent over the range of 50 to 200 kv., and additional filtration does not change the calibration curves observably.

In Figure 4, calibration curves for roentgen rays from the tube with 1.5 mm. of beryllium inherent filtration, and no added filtration, show the effect of thimble chamber type. In this comparison, three types of bakelite chambers (250 r, 100 r, and 25 r) were used in conjunction with r-meter, serial No. 1193. Another 25 r bakelite chamber was used in conjunction with r-meter, serial No. 1282. The readings of the two 25 r chambers and r-meters are the same, within experimental error, while those of the 100 r and 250 r chambers show substantially greater departure from those

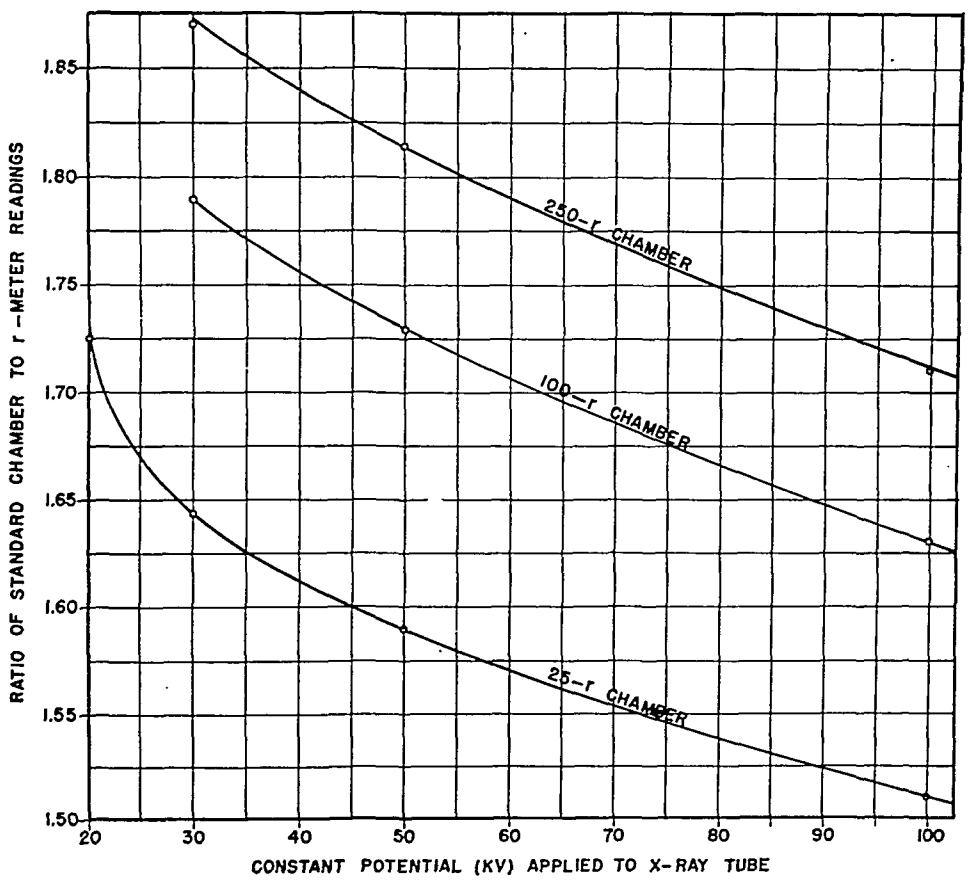


Fig. 4. The effect of roentgen-ray excitation potential upon the corrections required to the readings of different types of bakelite thimble chambers when calibrated on roentgen rays generated by a tube with 1.5 mm. of beryllium inherent filtration and no added filtration.

Note: The 250 r, 100 r, and 25 r chambers are each used in conjunction with r-meter No. 1193. Another 25 r chamber used in conjunction with r-meter No. 1282 yields readings which are the same within experimental error as those observed with the 25 r chamber which were read on r-meter No. 1193.

of the standard chamber. It is interesting to note that the calibration curves for these chambers run closely parallel to each other. For example, the correction factor to the 100 r and 250 r chambers are 1.63 and 1.71, respectively, at 100 kv., and 1.79 and 1.87, respectively, at 30 kv., or differences of 0.08 at each potential.

A 250 r nylon chamber with a 0.005 inch wall thickness has recently become commercially available, and its calibration is shown in Figure 5 using a roentgen-ray tube with 1.5 mm. of beryllium inherent filtration. For minimum-filtered radiation this chamber reads in error by 31.5 to 28 per cent over the range of 30 to 100 kv. This is in contrast with an error in the 250 r red bakelite chamber readings of 87 to 71 per cent in the same excitation potential range, as seen in Figure 4.

Table 1 shows the aluminum half-value layers for 10 to 200 kv. roentgen rays with filtration ranging from 1.5 mm. of beryllium to this plus 6 mm. of aluminum. For minimum filter the very very small half-value layers, even at 200 kv. indicate that the great part of the absorbed radiation is extremely soft, perhaps in the region of 20 to 30 kv., in terms of the usual measuring techniques. As an example of the effect of roentgen-ray beam quality upon thimble chamber calibration, it is observed in Figure 5 that 6 mm. of aluminum is required to reduce the correction factor to a minimum at 150 kv. Table 1 indicates that a 150 kv. beam, prefiltered by 6 mm. of aluminum, has a half-value layer of 7.6 mm. of aluminum. This is in contrast to half-value layers ranging from 0.04 to 0.18 mm. of aluminum at 10 and 200 kv., respective-

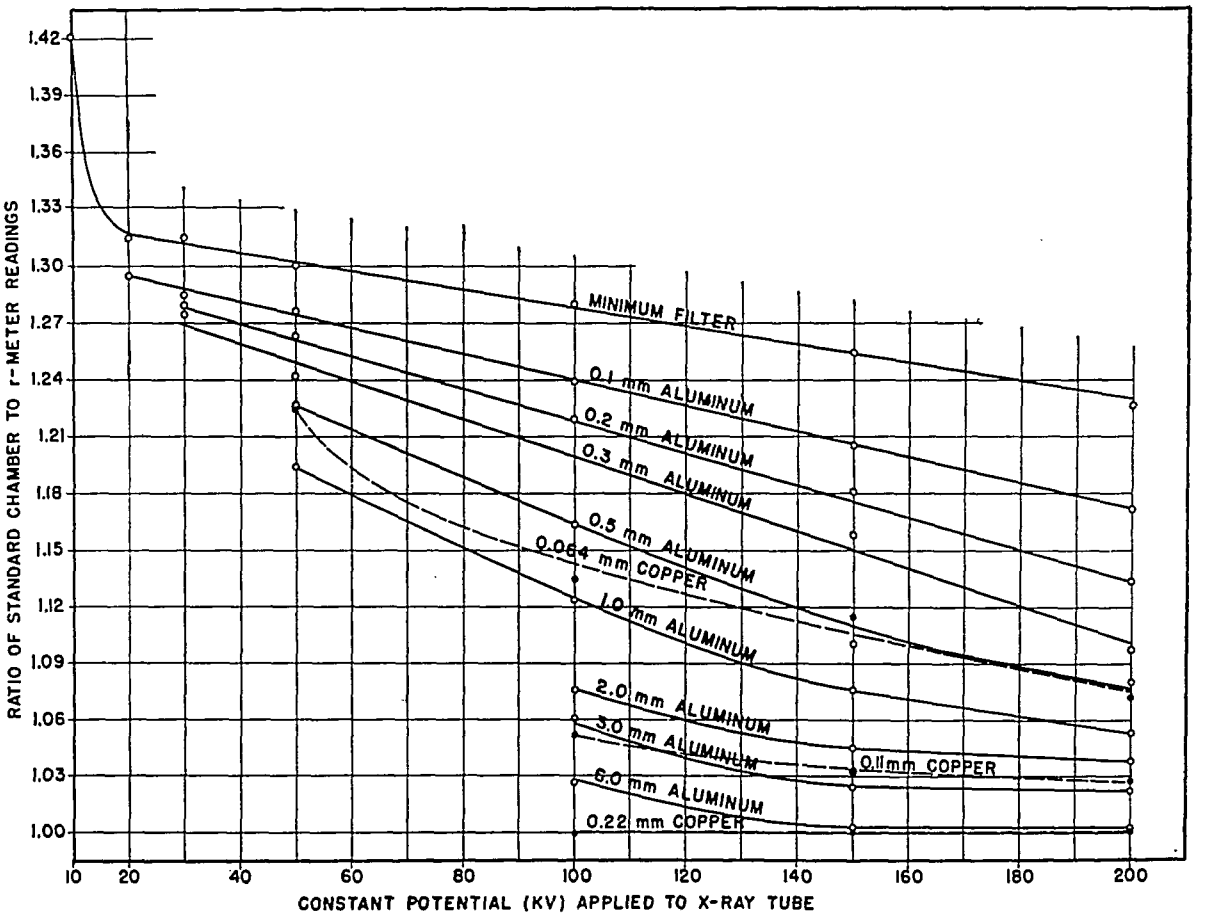


FIG. 5. The effect of roentgen-ray excitation potential and added aluminum and copper filtration upon corrections required to the readings of a 250 r nylon thimble chamber on r-meter No. 2449 when calibrated on roentgen rays generated by a tube with 1.5 mm. of beryllium inherent filtration.

TABLE I

ALUMINUM HALF-VALUE LAYER DETERMINED WITH FREE-AIR IONIZATION CHAMBER AS A FUNCTION OF FILTRATION AND OF ROENTGEN-RAY EXCITATION POTENTIAL

Constant Potential	Half-Value Layer of Aluminum								
	Minimum Filter*	Added Filter							
		0.1 mm. Al	0.2 mm. Al	0.3 mm. Al	0.5 mm. Al	1.0 mm. Al	2.0 mm. Al	3.0 mm. Al	6.0 mm. Al
(kv.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)
10	0.04	0.06	0.10						
20	0.08	0.11	0.15	0.18	0.22				
30	0.09	0.14	0.19	0.27	0.35	0.6	0.9	1.2	
50	0.10	0.15	0.29	0.34	0.57	1.0	1.4	1.9	2.8
100	0.11	0.19	0.37	0.48	1.0	1.8	2.9	3.6	5.3
150	0.14	0.29	0.64	1.2	2.0	3.2	4.6	5.5	7.6
200	0.18	0.40	1.3	2.1	3.4	4.6	6.3	7.1	8.8

* 1.5 mm. of beryllium plus 100 cm. of air.

for minimum filtered beams. In view of the large percentages of soft components in beams from beryllium-window tubes, it is to be expected that chambers used for measuring radiations from such tubes, with no added filtration will be very critical as to design characteristics.

III. CONCLUSION

Thimble chambers can be calibrated for use with the very low potential, lightly filtered radiations, such as produced by beryllium-window roentgen-ray tubes. However, the errors may be as large as 130 per cent for radiation produced at 10 kv. constant potential.

Considerable care must be exercised in determining the amount and kind of filtration and potential employed in thimble chamber calibrations for soft roentgen rays. These factors are relatively unimportant, however, where filtrations above 0.2 mm. of copper or about 6 mm. of aluminum are used.

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A NEGATIVE FEEDBACK DOSAGE RATE METER USING A VERY SMALL IONIZATION CHAMBER

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DURING the past few years several types of devices for measuring the radiation at a point have been described in the literature. Condenser chambers of very small physical dimensions have been developed.[1,7,9,10] These are especially useful for measuring the dose received at points within body cavities or even in the tissue surrounding radium implants. These chambers can be charged conveniently and subsequently measured by using an electrometer device developed by Spiers and Hay.[8] They are not particularly suited to the measurement of radiation at a large number of points within a phantom since the time taken to charge the chamber, place it in position, expose the chamber and finally measure the charge remaining on it can become appreciable. For such work a negative feedback direct current amplifier is useful.

Several amplifiers of this type have been described in the literature.[2,3,5] These devices all amplify and measure the small ionization current in an associated thimble chamber and so yield an instantaneous reading of the intensity of the roentgen-ray beam. If depth dose data are required such a chamber can be moved through a phantom while the intensity of the roentgen-ray beam is held constant. Devices using two thimble chambers have been developed[4] which avoid the need of holding the output of the roentgen machine constant. Most of these amplifiers require a rather large thimble chamber in order to obtain an ionization current large enough for amplification. This means of course that the intensity of radiation at a "point" cannot be measured. In this respect such devices are not as useful as the small condenser chamber.

In order to overcome this difficulty the authors have developed a highly sensitive D. C. amplifier using a very small ionization chamber. It cannot be claimed that this device is simple in nature but it does serve as a useful tool in a radio therapy department for measuring backscatter and depth dose and for the investigation of stray radiation about treatment cones. It will be used for the investigation of the depth dose obtainable with the 25 mev. betatron installed at the University of Saskatchewan. It has been in routine operation for about one year and has been found to be reliable in operation. The D.C. amplifier is capable of measuring currents down to 10^{-14} amperes, and in conjunction with an ionization chamber of 50 mm.^{3} volume has been used to measure radiation intensities of 5 r/min. to 500 r/min. with an accuracy of 1 per cent. For the higher dosage rates a chamber with a volume of 5 mm.^{3} has been used successfully. A photograph of the amplifier and a selection of the probes which have been used with it are shown in Figure 1. The 0–100 microammeter in the upper right hand corner is the meter on which the intensity of the roentgen-ray beam striking the thimble chamber is measured. The parts of the radiation meter will be described in turn.

The Probe. It is desirable to locate the thimble chamber near the electrometer tube to eliminate the effects of radiation on the sensitive electrode and to keep the time constant of the device small. The original probe *A* (Fig. 1) was made made as a unit but all the others shown in Figure 1 were constructed so that a selection of thimble chambers could be connected to the probe by means of a screw fitting. This greatly increases the usefulness of the device for

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† Graduate Student, University of Saskatchewan.

thimble chambers with special properties can be employed at will. In order to keep the probe small in volume the VX-41 tube manufactured by the Victoreen Instrument Company was used as the electrometer tube. It has a volume of about 1 cm.^{3} and excellent electrical characteristics, its input resistance when used in the space charge grid connection being about 10^{16} ohms. The electrical connections for the probe are shown in Figure 2.

It will be seen that the thimble chamber is connected so that the outer sheath is at ground potential while the sensitive central electrode is about 15 volts negative with respect to ground and connected to the space charge grid of the VX-41. The normal operating voltages of the VX-41 measured with respect to the filament are indicated. When radiation falls on the thimble chamber the ionization current which flows through the 10^{11} ohm resistor would cause a change ΔV in the potential of the point $\mathcal{Q}$ if the point P were at a fixed potential. However, the point P is connected to the output of the amplifier in such a way that it changes in potential by $-\Delta V$ of approximately the same magnitude so that the potential of $\mathcal{Q}$ remains almost constant regardless of the ionization current. This negative feedback characteristic of the amplifier makes the device linear in operation and insensitive to changes in the characteristics of the tube. It is important that an electrometer tube never be operated with the plate voltage applied before the filament is at operating temperature. Otherwise the tube becomes destabilized and will show very serious zero drift until it has been operated for several hours. For this reason a switch S is placed in the plate circuit of the VX-41. The parts of the electrometer cir-

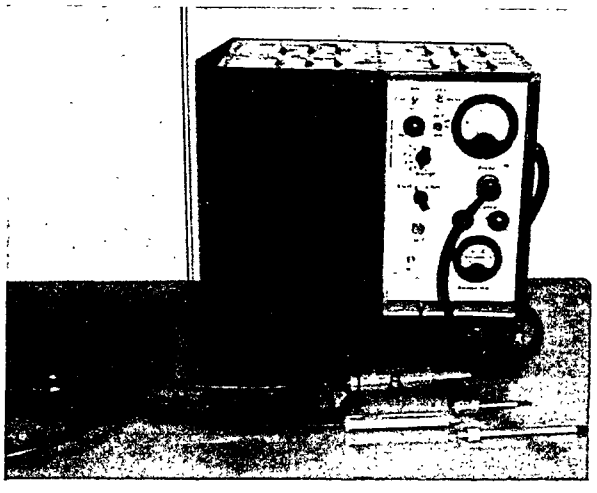


Fig. 1. Photograph of D.C. amplifier and probes.

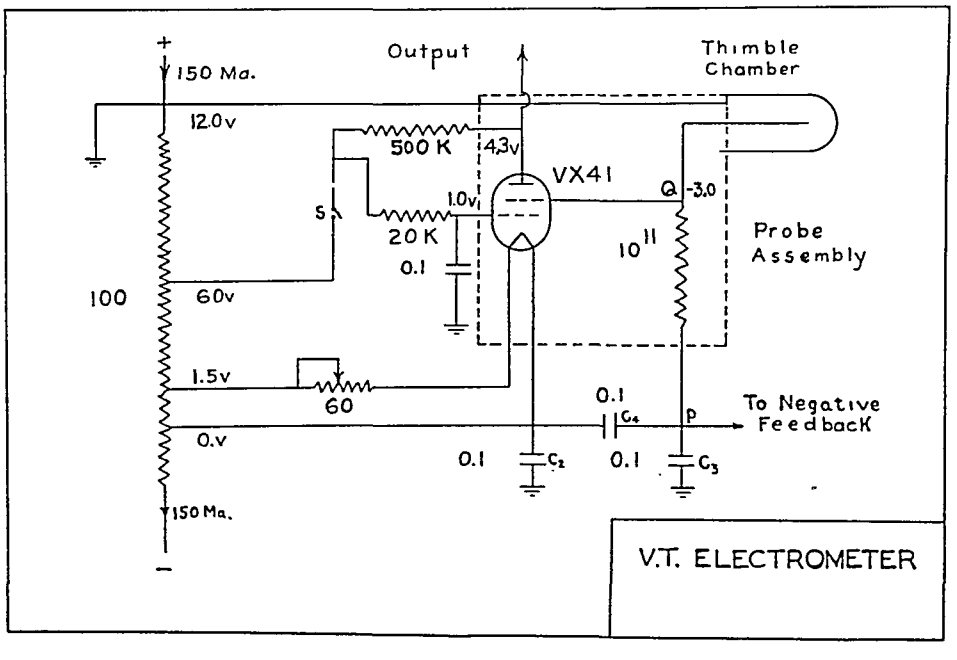


Fig. 2. Circuit diagram of vacuum tube electrometer circuit.

cuit which are situated in the probe are enclosed by the dotted line shown in Figure 2.

The actual mechanical construction of the probe is shown in Figure 3. The electrometer tube is located reasonably close to the ionization chamber and will at times be exposed to radiation. It is therefore necessary that the probe assembly be not affected by the radiation. Pockets of air trapped near the grid lead must be eliminated or the probe with a lead sheath 1/16 inch in thickness.

Power Supply and Amplifier. The power supply and amplifier shown diagrammatically in Figures 4 and 5 are based on a design originated by Miller.[6] Both circuits make use of the cathode control amplifier in tubes T_5 and T_6 of Figure 4 and T_2 and T_3 of Figure 5, for the elimination of cathode drift. One section of the twin triode

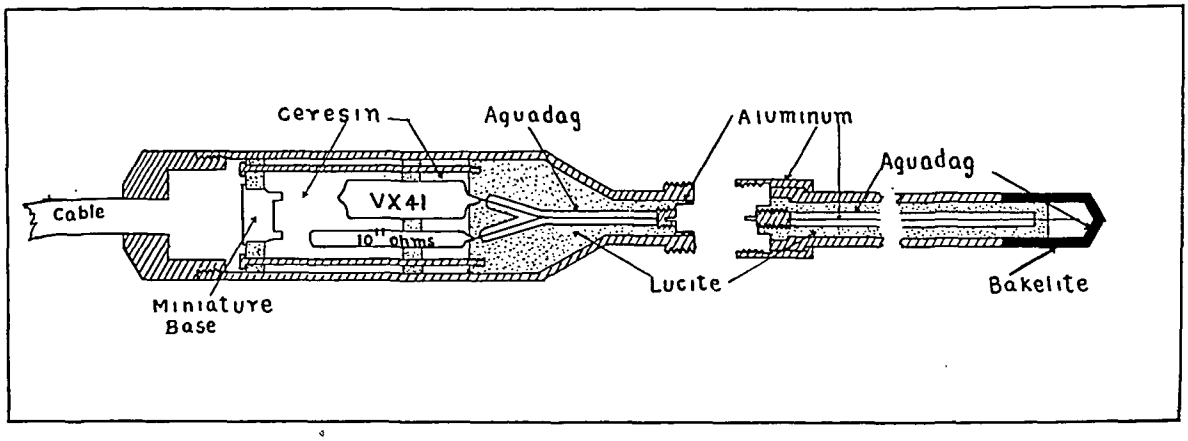


Fig. 3. Diagram of probe assembly.

enclosed in a field free region so that no ions can be collected. Therefore the grid lead is enclosed in a short piece of lucite tubing, coated with aquadag both inside and out, the outside surface being grounded and the inside connected to the grid. Ions produced in this region cannot be collected since they are in a field free region. The main volume of the probe is filled with ceresin wax of good insulating properties in order to exclude the air from around the tube and grid resistor. The probe without an ionization chamber was tested for radiation sensitivity using gamma rays, 400 kv. (peak) roentgen rays and 100 kv. (peak) roentgen rays. No deflection was observed for the gamma rays, a very small negative deflection when using 400 kv. (peak) roentgen rays and quite an appreciable deflection, using the softer roentgen rays. This effect is due likely to photoelectric emission from the grid of the VX-41. The effect was removed entirely by surrounding acts as the amplifier while the other section gives an inverse feedback, thus minimizing fluctuations due to changes in heater voltage, cathode emission, etc. Since a very accurately regulated power supply is necessary for the plate voltages of the tubes, it was decided to build one capable of operating the heaters of all critical tubes as well. For this reason the tube series which draws 150 milliamperes was chosen and the heaters of these tubes were placed in series with a bleeder chain (Fig. 2 and 5) from which voltages for the D. C. amplifier could be selected. The power supply of Figure 4 gives regulation to better than ± 1 millivolt for variations in the input voltage from 105 to 125 volts. This is quite adequate for the D. C. amplifier.

The signal from the VX-41 is amplified by tubes T_2 and T_3 (Fig. 5) and the amplified output is applied to one grid of the balanced cathode followers T_4 and T_5. The 0–100 output microammeter is connected

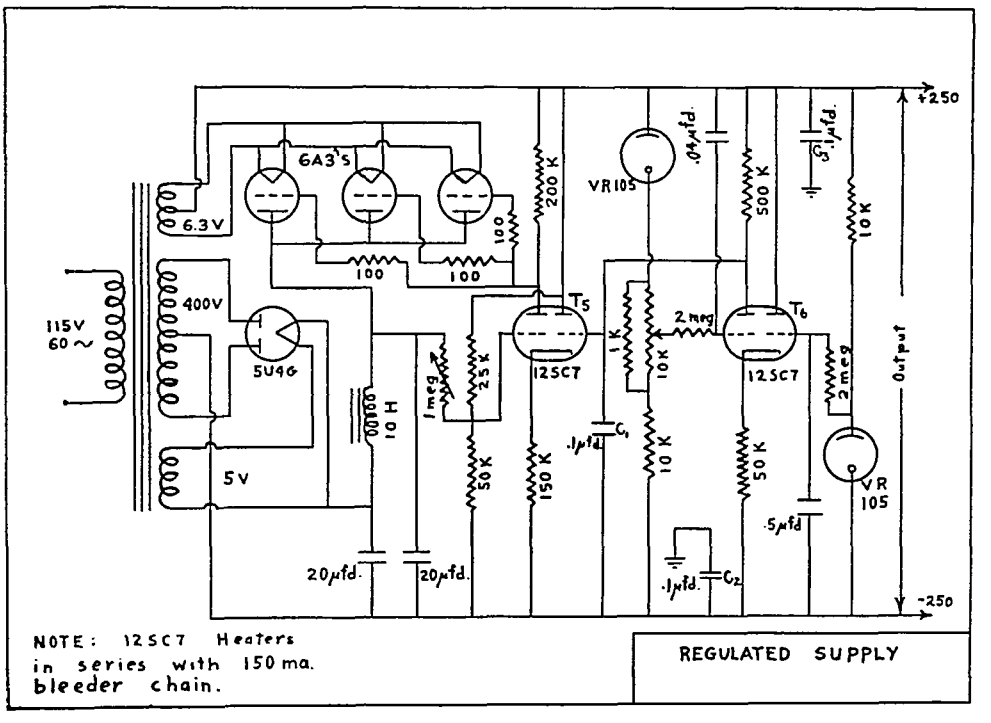


Fig. 4. Circuit diagram of regulated power supply for D. C. amplifier.

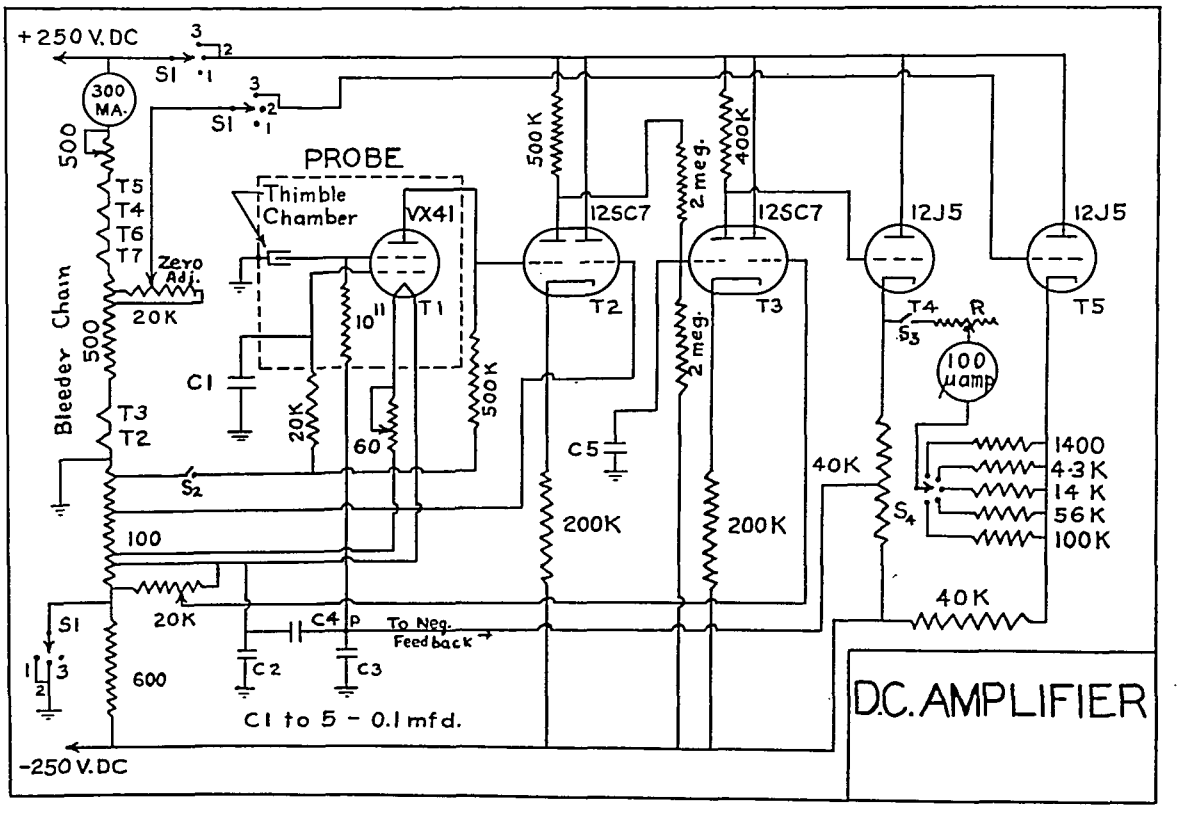


Fig. 5. Circuit diagram of D. C. amplifier.

between the cathodes of T_4 and T_5 through a rheostat R and range selector switch S_4. For zero ionization current the output meter is made to read zero by proper adjustment of the 20,000 ohm potentiometer to which the grid of T_5 is connected. Fifty per cent of the output from the cathode resistor of T_4 is fed back to the grid of the VX-41 so as to give negative feedback. Condensers C_2, C_3, C_4, and C_5 of Figure 5, and C_1, C_2, and C_3 of Figure 4 are necessary to ensure that negative feedback occurs for all frequencies. Without these troublesome oscillations occurred.

Before the power supply is turned on, S_1 (Fig. 5) is placed in position 1. This removes the section of the bleeder chain which supplies power to the VX-41 and removes the voltages from the plates of all the tubes in the amplifier. After the power supply starts to regulate as indicated by the small milliammeter (Fig. 1 and 5) S_1 may be moved through position 2 to 3. This applies voltage to the plates of the amplifier tubes and to the filament of the VX-41. After about one second, plate voltage may be applied to the VX-41 by closing S_2. Finally S_3 is closed and the zero adjustment made. After the radiation is turned on the proper range can be chosen by the selector switch S_4. For $R=0$, the five positions of S_4 give a full scale deflection for radiation intensities of about 5r/min., 15 r/min., 40 r/min., 100 r/min. and 300 r/min., respectively, using a thimble chamber of 50 mm.[3] Of course, other ranges can be obtained by placing different resistances in series with the meter. For depth dose work the variable resistance R is very convenient. Using it the output meter can be made to read 100 when the thimble chamber is at the surface of the phantom and the roentgen machine is giving a certain output. As the thimble is moved below the surface, percentage depth dose may be read directly off the output meter.

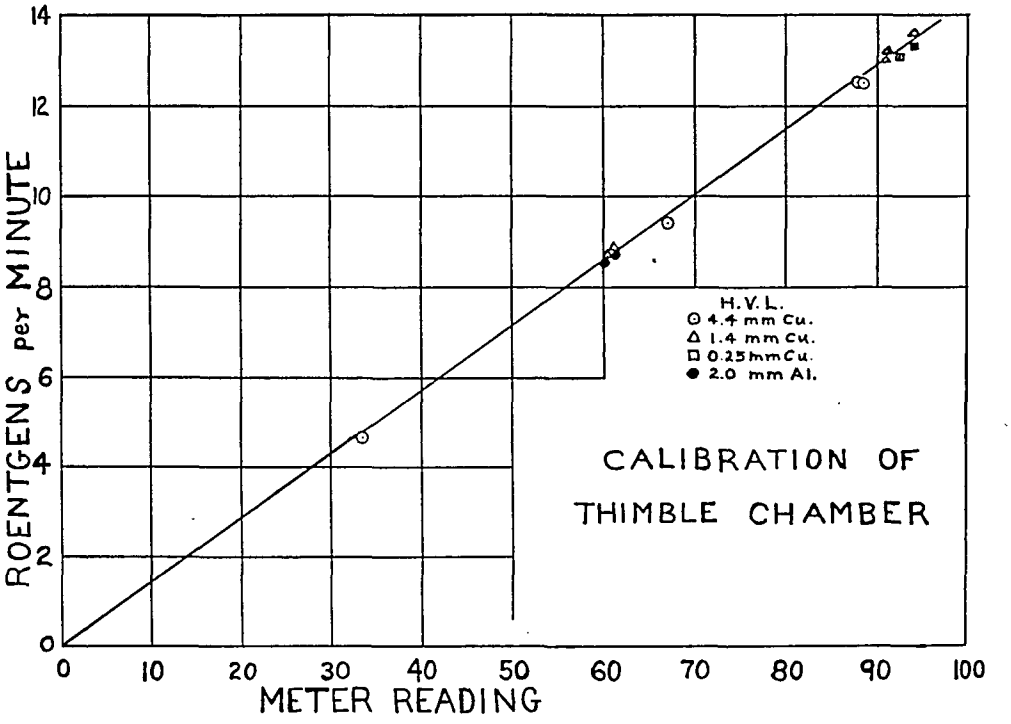


Fig. 6. Calibration of thimble chamber.

On the most sensitive range of the instrument erratic fluctuations amount to about 0.5 per cent of the full scale deflection. These are mainly due to thermal noise in the 10^{11} ohm resistor. When the amplifier is first turned on zero drift is troublesome but after about ten minutes

amounts to roughly 2 per cent per hour on the most sensitive range.

Linearity and Wavelength Dependence. Because of the large amount of negative feedback in the amplifier it would be expected that the instrument should be strictly linear. From examination of Table 1 and Figure 6 it will be seen that this is the case.

The wavelength dependence was checked against a Victoreen r-meter. The thimble chamber was constructed of red bakelite, coated on the inside with aquadag, and containing a central electrode of aluminum. By the proper choice of the size of central electrode it was possible to get a chamber which had the same response as the Victoreen. This is illustrated in Table 1 where the responses of the D.C. amplifier and the Victoreen are compared for four different qualities of radiation. The ratio of the readings on the two instruments, i.e. the sensitivity, is shown in the last two columns. It will be seen that for any one quality the sensitivity is constant regardless of the intensity of the radiation, indicating the linear response of the instrument. In the last column appear the average sensitivities for a given quality of radiation. This sensitivity varies somewhat with quality but the variation is hardly greater than the inherent error in the measurements would produce. The chamber has the same type of wavelength response as the Victoreen r-meter.

TABLE I

CALIBRATION OF THIMBLE CHAMBER

Half-Value Layer	D.C. Amplifier Reading R	Victoreen Reading r/min.	Sensitivity r/min/R	Average Sensitivity
	33.5	4.63	0.1405	
	67.0	9.41	0.1405	
4.4 mm. Cu	67.0	9.41	0.1405	0.1410
	88.0	12.45	0.1415	
	88.5	12.50	0.1415	
	60.5	8.70	0.1435	
	61.0	8.85	0.1450	
1.43 mm. Cu	91.0	13.2	0.1450	0.1442
	91.0	13.0	0.1430	
	94.0	13.6	0.1445	
0.25 mm. Cu	92.5	13.1	0.1420	0.1420
	94.0	13.3	0.1420	0.1420
2.0 mm. Al	60.0	8.57	0.1425	0.1422
	61.3	8.70	0.1420	

Uses of the Amplifier. The amplifier has been used for making depth dose measurements and measurements of backscatter. It has been found especially useful for investigating the distribution of radiation in a scattering medium in regions where the intensity of radiation changes rapidly. Because of the small size of the thimble chamber the device is particularly useful for this type of work. It is also useful for investigating stray radiation leaks about treatment cones. It is at present being used for the investigation of the depth doses obtainable with the 25 mev. betatron at the University of Saskatchewan. The results of these and other measurements will be reported later.

The authors wish to acknowledge the support which has been received from the National Research Council of Canada, the National Cancer Institute of Canada and the Saskatchewan Branch of the Canadian Cancer Society. They also wish to thank Professor E. L. Harrington, Head of the Physics Department, for his many helpful suggestions and Mr. A. H. Cox of the Physics Department Shop for his careful machine shop work.

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VOL. 61, NO. 4

DEPARTMENT OF TECHNIQUE

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ROENTGENOGRAPHIC FACSIMILE

A RAPID ACCURATE METHOD FOR REPRODUCING ROENTGENOGRAMS AT A DISTANCE VIA WIRE OR RADIO TRANSMISSION

By J. GERSHON-COHEN, M.D., *and* A. G. COOLEY
PHILADELPHIA, PENNSYLVANIA

THE roentgenologic service in hospitals of rural communities, in military outposts and in isolated mining and farming centers can seldom be arranged satisfactorily because the full-time attendance of a competent radiologist is not practical. These situations are now circumvented by obtaining the part time services of a radiologist in a nearby large community. By the use of roentgenographic facsimile, the full advantage of an experienced roentgenologist can be obtained at all times, thus affording rapid roentgenologic consultation whenever needed, including emergencies.

Since January 15, 1948, roentgenographic facsimile has been used daily in successful routine operation between the Chester County Hospital, West Chester, Pennsylvania, and the senior author's private office in Philadelphia, Pennsylvania, 28 miles distant. Whenever Dr. G. W. Brown, a graduate fellow in radiology, now training at the hospital, requires advice, he can transmit the facsimiles of the roentgenograms in question and, within a few

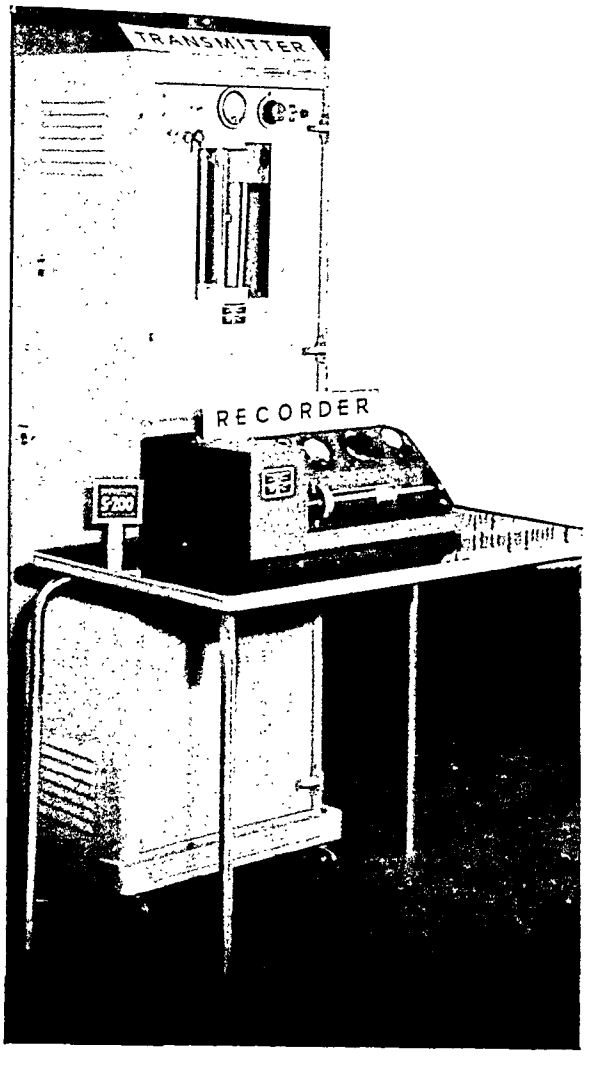


FIG. 1. The upright transmitter reveals the vertical glass drum on which is wrapped the roentgenogram. Inside this glass cylinder, an exciter lamp of the optical scanning system projects a beam of light through the glass and the enveloping film upon a photocell. Then through a special photocell circuit amplifier and synchronizing system, the signals are sent over commercial telephone circuits to the recorder similar to news-photo facsimile equipment. A special type of film is then exposed half the size of the original and quickly processed for interpretation.

minutes, engage in consultation with his senior, using the same telephone circuit over which the facsimiles were sent. Not only is this a valuable teaching aid, but it also quickly furnishes the patient's physician with an expert consultation and thus sustains his confidence in the over-all roentgenologic service. If a resident junior radiologist were not available, roentgenographic facsimile could be arranged so as to make possible direct quick consultation between the distant radiologist and the local referring physician. This has already been tried sufficiently to have established its practicality.

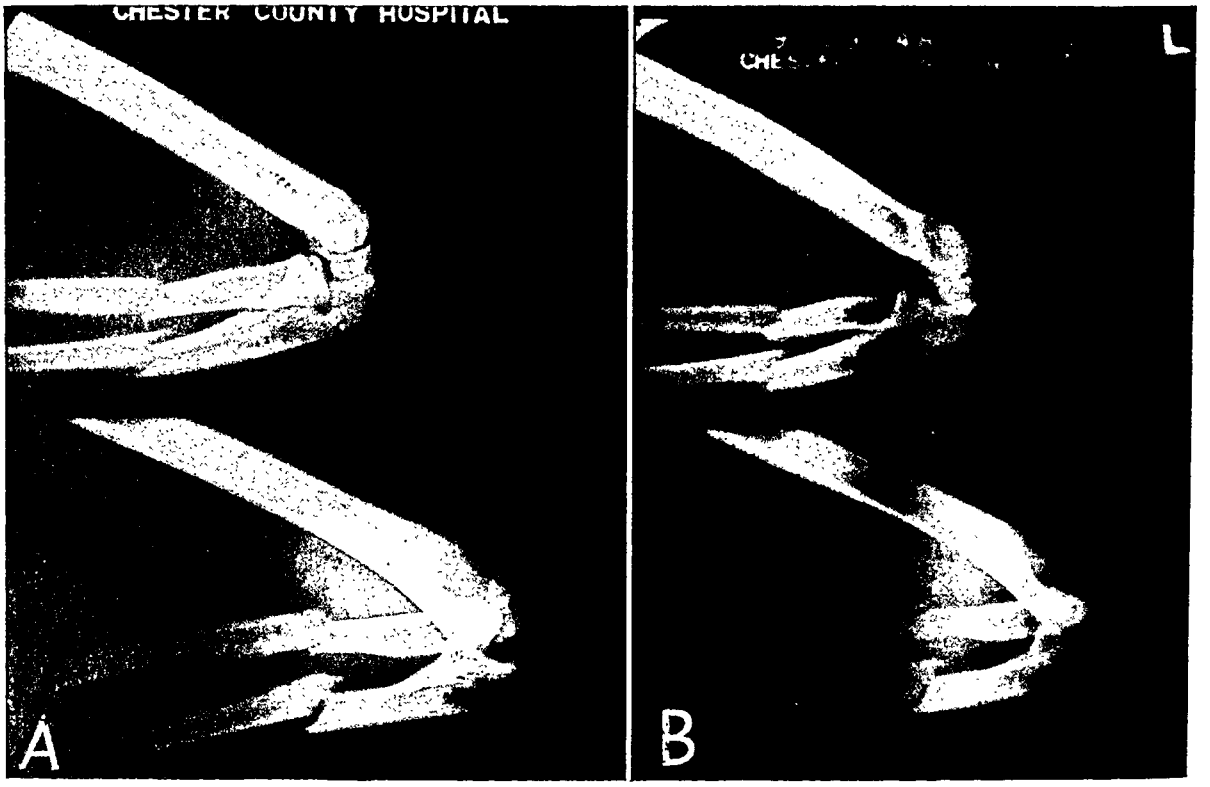


FIG. 2. *A*, fractures of bones of the forearm in original roentgenogram. *B*, facsimile of *A*.

The facsimile apparatus comprises a transmitter and a receiver. The roentgenogram to be copied is wrapped around a glass cylinder and held in place by an envelope of a simple clear plastic sheet. This cylinder rotates at 180 rpm. An optical scanning system projects a beam of light from an exciter lamp inside the cylinder through the wall of this glass cylinder and through the film onto a photoelectric cell. A special photocell circuit amplifier and synchronizing system is used, adopted from news-photo facsimile equipment now used by the newspapers and the Weather Bureau. The optical scanning system traverses the length of the drum so that 50 lines per inch are scanned. This enables transmission of a 14 by 17 inch film in slightly less than four minutes and smaller films in proportionately less time. The signals may be sent over telephone lines or radio circuits in the same way that wire photos or radio photos now are transmitted.

On the receiving apparatus, the negatives we use are half the size of the original roentgenograms. This recording film is of a type developed for wire-photo work by the Eastman Kodak Company and is known as E K Transmission Film, Type C. This film is easy to handle and it may be processed in ordinary solutions in about half the

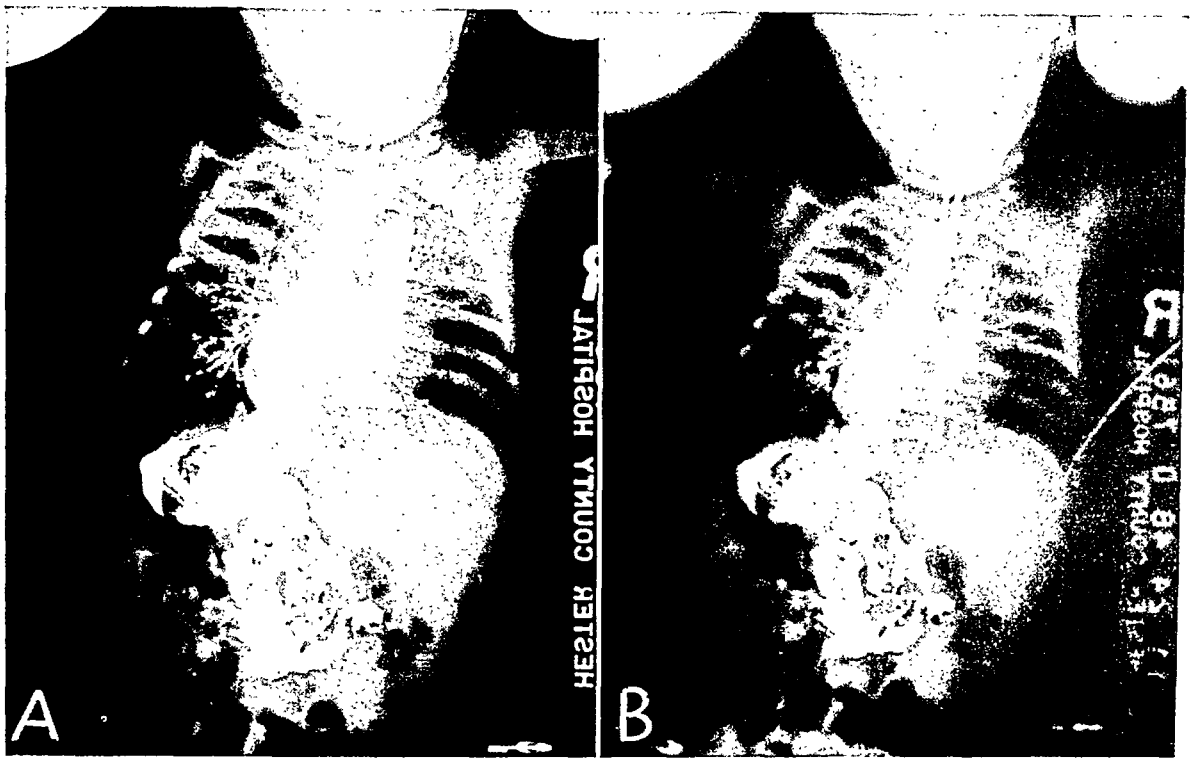


Fig. 5. *A*, lipiodol mapping of esophagus and tracheobronchial tree in case suspected of congenital defects in hypopharynx. No anatomical defects were found. *B*, facsimile of *A*.

time it takes to process regular roentgenograms. A very hot blast of air may be used for quick drying.

The facsimile retains all the detail of the original roentgenogram. Because of the half-sized reduction of the facsimile, many details in it are sharper and more easily noticed than in the original film.

It is estimated that the cost of installation and operation of this equipment will be economically sound when it becomes available. During World War II, equipment having signal characteristics similar to this type of roentgenographic facsimile was used in regular service between Washington, D. C. and Anchorage, Alaska. Excellent results were also obtained by the Office of War Information operated radio circuits over great distances, one of them between Chungking, China and Los Angeles, California.

It now seems probable that there will soon be available roentgenographic facsimile equipment which should prove to be a great aid in the solution of the problem of roentgenologic service for rural hospitals and various types of civilian and military medical outposts.

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EDITORIAL

GASTRIC VASCULAR SHUNTS

BARCLAY, in one of his thought-stimulating talks before the Faculty of Radiologists,[1,2] called attention to a number of pitfalls in the history of roentgenological diagnosis. He analyzed some of the lessons which have been learned over these many years and with prophetic vision pointed out a road to the future. He recalled that from its very beginning the roentgen ray was used as a method of study of the pathologic, and as a result, the roentgenologist was always looking for the abnormal, failing to appreciate to the fullest extent that he was also observing the normal. Barclay expressed regret that the anatomist in the early days of the roentgen ray had not appreciated its value in application to the anatomical studies of the viscera in the normal living subject, and also that the schools of physiology failed to appreciate to the fullest the value of roentgenology as an aid in studying the gastrointestinal tract.

No one is perhaps better equipped than Barclay to have pointed out these glaring defects. He has throughout the years stood at the forefront of his profession and has contributed enormously to an elucidation of the pathological problems with which the roentgenologist has to deal. He has recently made brilliant contributions to anatomy and physiology in his studies of the renal circulation and more recently has reported his epoch-making studies on the gastric vascular shunts. Barclay has throughout the years championed the thought that the proper approach to a study of any pathologic state must be had through a proper understanding of the normal.

In a recent issue of the *British Journal of Radiology*, Barclay and Bentley[3] in a report of their studies on "The Visualisation of the Human Stomach: A Preliminary Note on the Shunting Effect of Trauma" have demonstrated anew the important lesson of the worthwhileness of intimate anatomical studies of the normal. In the course of their investigation into the blood vessels of the ulcerated stomach it became evident that the circulation through the gastric vessels is modified as a result of the conditions of the surgical operation. The mucous membrane of stomachs removed at operation is observed to be excluded from the active circulation in the stomach wall, further studies indicating that this is brought about by an arteriovenous shunt, similar to that described by Trueta and associates[4] in the kidney. As a result of their studies, Barclay and Bentley produced evidence of the existence of a system of arteriovenous anastomoses in the submucosa of the stomach wall, and they postulate that these shunts are probably under sympathetic control; their opening by nervous stress or trauma will deprive the mucosa of its vital blood stream.

In order that the arteries and their branches might be demonstrated down to the arterioles, a proprietary preparation of bismuth oxychloride ("Chlorbismol"), 20 per cent, was used as the contrast medium,

[1] Barclay, A. E. Radiology—empiricism or science? *Brit. J. Radiol.*, 1943, *16*, 344–347.

[2] Roentgenological problems, past and future. Editorial. AM. J. ROENTGENOL. & RAD. THERAPY, 1944, *51*, 96–97.

[3] Barclay, A. E., and Bentley, F. H. The visualisation of the human stomach; a preliminary note on the shunting effect of trauma. *Brit. J. Radiol.*, Feb., 1949, *22*, 62–67; also *Gastroenterology*, Feb., 1949. Also, Gastric vascular shunts. *Lancet*, Feb. 12, 1949, *1*, 267–268.

[4] Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J., and Prichard, M. M. L. Studies on the Renal Circulation. Blackwell Scientific Publications, Ltd., Oxford, 1947.

injected into one of the gastric or gastro-epiploic arteries. This mass was chosen because it has a particle size too large to enter the capillaries, and it outlines the larger vessels perfectly. Such injection in the cadaver stomach shows that the larger arteries divide during their passage through the stomach wall to form a main plexus of smaller arteries lying in the submucous layer between the muscle coat and the mucosa, over the whole stomach wall. These anastomoses are of large size and are readily seen, and moreover they are so profuse that an injection through a single gastric or gastro-epiploic artery suffices to fill the whole vascular anastomotic plexus of both anterior and posterior stomach walls, and also the other gastric and gastro-epiploic arteries by retrograde injection.

They found that it was necessary to use an injection mass of smaller particle size in order to demonstrate the peripheral vascular supply. This consists of finer vessels arising from the main plexus. For this purpose colloidal silver iodide, 10 per cent, was used. The small arterioles and capillaries when filled with this contrast medium are seen quite clearly in micro-arteriographs. Cadaver preparations in which this mass was injected show that smaller vessels arise from the main plexus and run through the submucosa and the muscularis mucosae towards the under aspect of the mucous membrane, where they anastomose with each other to form an intricate plexus of finer vessels, close to the mucous membrane.

From this plexus arises a rich vascular network supplying the gastric mucosa, formed from large numbers of fine arterioles which then break up into capillaries. These vessels run perpendicularly through the mucosa toward the surface, and their appearance in a micro-arteriograph is very striking.

Barclay and Bentley observed that when the arteries of stomachs removed at operation were injected with colloidal silver iodide at the same pressure and using the same technique as in the cadaver, there was an important difference compared with the cadaver stomach. Whereas in the latter the vessels of the mucosa were filled over wide areas, in the operation specimens it was difficult to find an area of mucous membrane in which the injection mass had reached the peripheral circulation at all. While the technique of the injection was identical in the two varieties of stomachs, in no instance was it possible to outline the vessels of the mucosa, that is the peripheral circulation, in twelve specimens removed at operation except in occasional small and very inadequately filled areas.

The appearances obtained in these operation specimens suggested either that there was some impediment to the entry of the injection mass into the peripheral circulation in the mucosa in the operation specimens, or that the injection flowed from the arteries of the submucosal plexus directly into the gastric veins by some easier channel than that afforded by the mucosal network; in short, from this observation there appeared to be an arteriovenous anastomosis, or shunt, located in the submucous plexus.

The investigators thought that the conditions under which the stomachs were removed at operation would favor the action of any shunt, if one existed. Thus, opening of the peritoneal cavity to the air, manipulation of the stomach and traction on its mesenteries would all inflict a degree of trauma, while the application of clamps would then effectively cut off the nerve supply. From the observations gained from their work on the renal circulation, they thought that such a degree of stimulation might open up arteriovenous shunts reflexly, and the application of clamps would fix the peripheral vascular pattern in the shunted condition.

They thought that if such a shunt were to exist functionally, then it must be almost complete in its action to account for the practically total emptiness of the mucosal vessels. With this thought in mind, they made observations at six operations on the surface veins of the stomach from

the moment when the peritoneal cavity was opened, taking care that the oxygenation of the patient remained at a constant level. They observed that the veins coursing along the anterior wall of the stomach changed in color during the first two or three minutes after the peritoneum was opened, from purple-blue to a dusky pink. While this color change was occurring, samples of blood were taken from a venous tributary running toward the lesser curvature of the stomach as quickly as possible after the peritoneum was opened. A second sample was taken from an adjacent vein three minutes later when the color change was apparent. The blood was aspirated directly into potassium oxylate solution, and the percentage oxygen saturation of the hemoglobin determined by the method of Kramer. The percentage saturation of the first sample of blood removed was 74 per cent and of the second sample 91 per cent. Such a rapid change in oxygenation suggested strongly a direct passage of blood from the arterial to the venous side must have occurred through an arteriovenous shunt.

The investigators thought that if such a shunt is brought into play by opening the peritoneal cavity and trauma to the stomach, it should be possible to modify the shunt or to prevent its occurrence by blocking the sympathetic nerves to the stomach before the operation is begun. This thought was brought about by the fact that it is known from their work on the renal circulation that the arteriovenous anastomoses in the kidney are under the control of the autonomic nervous system.

In order to test the correctness of this postulate, a patient upon whom a gastrectomy was to be performed was anesthetized with a combination of general and high spinal anesthesia. The spinal anesthetic ascended to the level of the first and second thoracic vertebrae and the systolic pressure fell from 145/85 to between 80/40 and 40/? throughout the operation. The vessels of the excised stomach were injected with colloidal silver iodide in the usual way. The resulting micro-arteriograph showed a remarkable difference compared with all the other injected operation specimens. In this stomach the mucosal vessels were abundantly filled in all areas of the stomach wall that were reached by the injection, giving the appearance of complete filling of the mucosal vessels.

Blocking of the sympathetic outflow throughout the operation had been followed by an extensive circulation through the mucous membrane in marked contrast to the absence of circulation to these vessels when the sympathetic pathways were intact.

The investigators concluded from these observations that in the wall of the stomach there are arteriovenous anastomoses in the region of the submucous plexus of vessels, whose opening excludes active circulation through the vessels of the mucous membrane. They further concluded that when the peritoneal cavity is opened and the stomach handled at operation, the shunt comes into play, and this condition persists in the excised stomach wall after the operation. These observations are consistent and agree with those made by Trueta and associates that the vascular pattern of the shunts within the kidney persists after the supplying vessels have been clamped and the nerve supply cut off.

From these studies the investigators adduced evidence indicating that the arteriovenous anastomoses in the stomach wall are under the control of the autonomic nervous system, for when the sympathetic outflow to the stomach is blocked by means of a spinal anesthetic the shunts do not open, and injection of the stomach vessels reveals filling of the extensive blood supply of the mucous membrane.

All of this epoch-making work is made possible by Barclay's[5] brilliant technical achievement in his development of micro-arteriography for without this, such a dis-

[5] Barclay, A. E. Micro-arteriography. *Brit. J. Radiol.*, 1947, *20*, 394–404; also, Am. J. Roentgenol. & Rad. Therapy, 1948, *60*, 1–12.

covery would not have been possible.

This report of Barclay and Bentley is a "preliminary note" and obviously further studies must and will be made. But this latest contribution is a great tribute to Barclay's perseverance in the investigation of his first love, namely the normal. These epoch-making studies of Barclay and his associates were carried on in spite of Dr. Barclay's serious illness, and after fifty years of contribution to the progress of roentgenology, he makes observations on a study of the normal which have untold possibilities in elucidating some of the pathologic problems such as the sudden formation of peptic ulcers and the acute penetrating or perforating ulcers of the stomach and duodenum which are seen frequently. This brilliant work opens up great possibilities not only in explaining some of the causative factors in ulcer formation but may ultimately be of great benefit in the cure of gastric and duodenal ulcers.

Barclay in this outstanding contribution brings again to the fore his emphasis of a need of well equipped research departments in the universities closely allied with the departments of anatomy, physiology and clinical medicine, having access also to the department of radiology of the hospital. Barclay conceived such research institutes as an imperative need and in his opinion they should be staffed by men with clinical experience in roentgenologic work. Certainly his brilliant contributions in these later years have justified such a conception of a great research institute.

VOL. 61, NO. 4

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

AMERICAN RADIUM SOCIETY
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1949, to be announced.

AMERICAN COLLEGE OF RADIOLOGY
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: Atlantic City, N. J., June 8–10, 1949.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Next meeting time and place of Alabama State Medical Association, Montgomery, Ala., April 19–21, 1949.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. A. H. Levy, 1354 Carroll St., Brooklyn 13, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. Merthyn A. Thomas, 10515 Carnegie Ave. Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday of October and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

HOUSTON X-RAY CLUB
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA X-RAY CLUB
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

LOUISVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

Nebraska Radiological Society
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

Northern California Radiological Club
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August.

Ohio State Radiological Society
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual Meeting: May 20 and 21, 1949, Bedford Springs Hotel, Bedford, Pa.

Philadelphia Roentgen Ray Society
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Queens Roentgen Ray Society
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Robert M. Lowman, Grace-New Haven Community Hospital, New Haven 11. Meets bimonthly second Thursday, at place selected by Secretary.

Radiological Section, District of Columbia Medical Society
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of New Jersey
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Ralph E. Alexander, 101 Medical Arts Bldg. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Denver, Colo., August 18, 19, 20, 1949.

St. Louis Society of Radiologists
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

Section on Radiology, California Medical Association
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. Ivan J. Miller, 49 Fourth St., San Francisco 3. Meets monthly on third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Langley Porter Clinic, University of California Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 p.m.
Medical Members' meeting, on third Friday in each month at 5:00 p.m., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 2100 Marlowe Ave., Montreal 28, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad.
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 p.m.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

PRELIMINARY PROGRAM

American Radium Society

THE following is the preliminary program which has been arranged for the Thirty-first Annual Meeting of the American Radium Society to be held at the Ambassador Hotel, Atlantic City, New Jersey, Sunday, Monday and Tuesday, June 5, 6 and 7, 1949.

Sunday Morning, June 5, 1949

1. Lay Propaganda. Affirmative—Charles Cameron, M.D., New York, N. Y. Negative—Daniel Blain, M.D. (by invitation), Washington, D. C.
2. State Control of Cancer. Herman Hilleboe, M.D., and M. L. Levin, M. D. (both by invitation), Albany, N. Y.
3. Federal Cancer Control Activities. Austin V. Deibert, M.D. (by invitation), Washington, D. C.

Monday Morning, June 6, 1949

1. Presidential Address. Maurice Lenz, M.D., New York, N. Y.
2. Planning the Radioisotope Program in the Hospital. Edith H. Quimby, D. Sc., and Carl Braestrup (by invitation), New York, N. Y.
3. Radioactive Colloidal Gold. Alfred I. Sherman, M.D. (by invitation), St. Louis, Mo., and James Nolan, M.D., Los Angeles, Calif.
4. Beta Radiation in Superficial Lesions of the Eye. Charles Iliff, M.D. (by invitation), Baltimore, Md.
5. Roles of Surgery and Radiation in the Treatment of Cancer. L. H. Garland, M.D. (by invitation), San Francisco, Calif.

Monday Afternoon, June 6, 1949

1. Cancer of the Lung. John Pool, M.D., New York, N. Y.
2. Primary Cancer of the Vagina. Robert E. Fricke, M.D., H. H. Bowing, M.D., and D. G. Decker, M.D. (by invitation), Rochester, Minn.
3. The Planning of Irradiation in Cancer of the Uterus and Cervix. Gilbert Fletcher, M.D. (by invitation), Houston, Texas.
4. Individualized Interstitial Irradiation of Carcinoma of the Uterine Cervix Using Cobalt^{60} in Needles Inserted through Lucite Templates: A Progress Report. Joseph L. Morton, M.D., Allan C. Barnes, M.D., and George W. Callendine, M.D. (all by invitation), Columbus, Ohio.

JANEWAY LECTURE. Low Intensity of Radiation Element Needles. Charles L. Martin, M.D., Dallas, Texas.

Tuesday Morning, June 7, 1949

1. Endocrine Therapy in Breast Cancer. Roy Hertz, M.D. (by invitation), Washington, D. C.
2. Cancer of the Thyroid. Hugh F. Hare, M.D., Boston, Mass.
3. Radioactive Iodine I^{131} in Diagnosis and Treatment of Toxic Goiter. Sidney Werner, M.D. (by invitation), New York, N. Y.
4. Remote Controlled Radium Emanation Plant and Automatic Measuring Apparatus for Gold Implants. John E. Rose, M.D., Chicago, Ill., and Robert W. Swain (both by invitation), Baltimore, Md.
5. Harmful Effects of Irradiation. W. E. Chamberlain, M.D., Philadelphia, Pa.

Tuesday Afternoon, June 7, 1949

Lymphoma Symposium

LLOYD F. CRAVER, M.D., *Chairman*

1. Interrelationships of Malignant Lymphomas. Philip Custer, M.D. (by invitation), Philadelphia, Pa.
2. Treatment of Myeloma by Urethane. Wayne Rundles, M.D. (by invitation), Durham, N. C.
3. Review of Chemotherapy for Leukopenias and Lymphomas. William Dameshek, M.D. (by invitation), Boston, Mass.
4. Review of Isotope Therapy for Leukemia. E. H. Reinhard, M.D. (by invitation), St. Louis, Mo.
5. Advances in Therapy of Hodgkin's Disease. Frank Bethell, M.D. (by invitation), Ann Arbor, Mich.

SIXTH INTERNATIONAL CONGRESS OF RADIOLOGY

The Sixth International Congress of Radiology will be held in London from July 23 to July 30, 1950. The headquarters of the Congress will be at the Central Hall, Westminster, which will also house an extensive Scientific Exhibit. The Technical Exhibit of apparatus will be located in the Halls of the Royal Horticultural Society nearby.

The Officers of the Congress are as follows:

President—Dr. Ralston Paterson, Manchester.
President-Emeritus—Dr. A. E. Barclay, Oxford.
Vice-Presidents:
Diagnosis—Dr. S. Cochrane Shanks, London.
Therapy—Prof. B. W. Windeyer, London.
Biology—Dr. F. Gordon Spear, Cambridge.
Physics—Prof. W. V. Mayneord, London.
Treasurer—Dr. H. Graham Hodgson, London.
Secretary-General—Dr. J. W. McLaren, London.

The subjects chosen for the main scientific meetings are:

1. General Congress Scientific Meetings.
 (a) "Radiological Achievement, 1937–1950."
 (b) "Mass Radiology of the Chest."
 (c) "Supervoltage Radiotherapy."
 (d) "Radiation Hazards."
2. Diagnosis Section Symposia.
 (a) "Skeletal Changes in Blood Diseases."
 (b) "Radiology of the Small Intestine."
 (c) "Arthrography."
 (d) "Angio-cardiography."
3. Therapy Section Symposia.
 (a) "Method of Presentation of Results of Treatment."
 (b) "Radioactive Isotopes."
 (c) "Cancer of the Larynx."
 (d) "Cancer of the Breast."
4. Biology Section Symposia.
 (a) "Radiation Histology."
 (b) "Radiation Chemistry."
 (c) "Radiation Genetics."
 (d) "Mode of Action of Ionizing Radiations."
5. Physics Section Symposia.
 (a) "Acceleration of Particles and the Generation of Ionizing Radiations."
 (b) "Radiological Units."
 (c) "Radiotherapeutic Physics."
 (d) "Production and Physical Properties of Radioisotopes."

Selected speakers will be invited to contribute the major portion of these symposia. Other sessions will be devoted to the reading of papers proffered by authors on their own topics.

A varied and interesting social programme is being arranged for members of the Congress, and special attention is being paid to the entertainment of Associates accompanying Members.

During the week preceding and the two weeks following the Congress, demonstrations will take place in the radiological departments of a number of London hospitals. Planned tours to centres of interest in Great Britain and Ireland are being arranged to follow the Congress; they will include excursions to the neighbouring countryside by coach, visits to buildings of historical interest, demonstrations at hospitals, and a full social programme.

Those wishing to attend the Congress as Full Members (£7.7s.0d.) or as Junior Members (under thirty years of age on January 1, 1950—£4.4s.0d.) must be members of a radiological society, or sponsored by a radiological society. Ladies and children accompanying Members can be registered as Associate Members (£3.3s.0d.). Associate Membership is also open to technical staff of radiological departments and laboratories, or of the X-ray industry. A late fee will be charged to those registering after April 1, 1950.

Members of the Congress may make their travel and hotel reservations through any office of Messrs. Thomas Cook & Son, Ltd. (or their associated company, the Cie Internationale des Wagon-Lits) who have been appointed the official travel agents for the Congress.

It is planned to issue a detailed Programme with registration forms to the members of radiological societies in April, 1949. All communications in connection with the Congress should be addressed to the Secretary-General at 45 Lincoln's Inn Fields, London, W.C.2.

Note: It has just been learned that H.R.H. The Princess Elizabeth hopes to open the Congress.

BROOKHAVEN NATIONAL LABORATORY NUCLEAR REACTOR

The construction of a nuclear reactor (atomic pile) and auxiliary laboratories is nearing completion at Brookhaven National Laboratory, and initial operation is expected in the fall of 1949. The reactor has been designed to provide a unique facility to serve the needs of the scientific, engineering, and industrial institutions located in the northeastern part of the United States. One of the major design considerations was that the reactor should be able to support an extensive research program. Emphasis has been placed on reliable, safe, and continuous operation.

The reactor is an air-cooled unit constructed of graphite and unenriched uranium. The maximum thermal neutron flux is expected to be about 5×10^{12} neutrons per square centimeter per second. For experiments, one hole 12 inches square, and several 4 inch square holes penetrating the shield at various levels, will permit the insertion of apparatus in the interior of the reactor and the release of collimated neutron beams. The over-all width of the reactor, including the shield, is about 38 feet in the direction of the 4 inch openings. A number of automatic devices will allow controlled irradiation of samples for periods as short as ten seconds. The top shield of the reactor consists of removable 4 foot square blocks. It will accommodate thermal columns and large equipment designed to utilize leakage thermal neutron flux (in excess of 10^{11} neutrons per square centimeter per second). Provision has been made for cages in which large size laboratory animals can be moved under the reactor. It will be possible to conduct research on three vertical faces of the reactor, as well as at the top and bottom.

Laboratories specially designed for handling radioactive materials are included in the reactor building. They will accommodate more than eighty scientists and technicians for research in physics, chemistry, biology, and medicine.

A "hot" laboratory is being constructed near the reactor building; the structure will be linked by a monorail and by pneumatic tubes for transporting irradiated material. Three distinct facilities will be provided in the "hot" laboratory: (1) "hot cells" for remote control processing of samples having up to 50 curies of 2 mev. gamma activity; (2) "semi-hot cells" for handling samples having 1 millicurie to 1 curie of 2 mev. gamma activity, using semiremote control techniques, including tongs and special manipulators; and (3) a "semi-works" area in which large apparatus can be erected with appropriate shielding. The "hot" laboratory building will also include analytical laboratories, shops, store rooms for "hot" and "cold" materials, personnel locker space, and offices. Its completion will be deferred until after the completion of the reactor.

BASIC COURSES IN TECHNIQUES OF USING RADIOISOTOPES AS TRACERS

The Special Training Division of the Oak Ridge Institute of Nuclear Studies announces that three basic courses in the techniques of using radioisotopes as tracers will be held during the summer. In addition tentative plans are being made for two secondary courses in this field.

The basic courses will be similar to a series of seven courses offered at Oak Ridge last summer and during the fall and winter months. Thirty-two participants will be accepted for each of the four-week courses. Each session is divided into laboratory work, lectures on laboratory experiments, general background lectures, and special-topic seminars. In order to give participants a maximum of knowledge and ability in the handling of radioactive isotopes in research, experiments will be conducted covering the use and calibration of instruments, and the purification and separation of radioactive materials from

inert materials and from other radioactive materials. Other laboratory periods will be devoted to the application of various radioisotope techniques. Ample time will be allowed for library work and conferences with the staff on individual problems.

Seminar topics include the use of radioisotopes in animal and human experimentation, principles and practices of health physics, design of radiochemical laboratory, dosimetry, instrumentation, and the effects of radiation on living cells.

The basic courses will be given from June 6 to July 1, July 11 to August 5, and from August 8 to September 2, 1949.

Applications for these courses should be mailed prior to June 1 if possible.

The two secondary courses will be of two weeks' duration and will be open to research workers who have completed the basic course or its equivalent in actual radioisotope work. These courses will be combined symposia and practical sessions in new techniques. One of the two courses, set tentatively for the period September 5–16, 1949, will be devoted primarily to the use of radioisotopes in medical research. Typical work covering the use of sodium, iodine, phosphorus, etc., in medical use will be included in the course. The other course, tentatively scheduled for the period September 19–30, will be concerned primarily with instrumentation. New developments in circuitry, scintillation counters and crystal counters will be taken up in some detail. A competent staff assembled from the field will conduct the secondary courses. Enrollment for the two courses will be limited, and interested individuals should establish contact with the Institute as soon as possible.

A registration fee of $25.00 will be charged for the basic courses. The fee for the secondary courses has not been determined as yet. Dormitory facilities in Oak Ridge, including linen, towels, etc., will be provided at a nominal cost, and food may be obtained in cafeterias and restaurants.

Additional information on the courses and application forms may be obtained from Dr. Ralph T. Overman, Chairman, Special Training Division, Oak Ridge Institute of Nculear Studies, P. O. Box 117, Oak Ridge, Tennessee.

TWENTY-FIFTH ANNIVERSARY OF RADIATION THERAPY DEPARTMENT OF BELLEVUE HOSPITAL

The Twenty-fifth Anniversary of the establishment of the Radiation Therapy Department of Bellevue Hospital under the direction of Dr. Ira I. Kaplan was marked by a special clinical gathering of the Department's Alumni, on March 24, 1949, with lectures by Dr. Bradley L. Coley, "Bone Tumors—A Field Requiring Cooperation Between the Radiologist and the Surgeon"; Dr. Douglas Quick, "Advances in Radiation Therapy in the Past Twenty-Five Years," and Dr. I. C. Rubin, "Twenty-Five Years' Experience with Radiation Treatment for Sterility Associated with Habitually Delayed Periods." Luncheon was followed by clinical demonstration of the work of the department, and the celebration concluded with a Testimonial Dinner to Dr. Kaplan.

DAVID ANDERSON-BERRY PRIZE (1950)

A David Anderson-Berry silver-gilt medal, together with a sum of money amounting to about £100, will be awarded in 1950 by the Royal Society of Edinburgh to the person, who, in the opinion of the Council, has recently produced the best work on the therapeutic effect of roentgen rays on human diseases.

Applications for this prize are invited. They may be based on both published and unpublished work and should be accompanied by copies of relevant papers.

Applications must be in the hands of the General Secretary, Royal Society of Edinburgh, 22 George Street, Edinburgh 2, Scotland, by March 31, 1950.

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

Department Editor: George M. Wyatt, M.D., 1835 Eye St., N.W., Washington 6, D. C.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Neck and Chest

Olsen, A. M.: Esophagitis 573
Gross, R. E., and Neuhauser, E. B. D.: Compression of the trachea by an anomalous innominate artery 573
Evans, T. C.: Preparation of radioautographs of thyroid tumors for study at high magnification 574
Quimby, E. H., and McCune, D. J.: Uptake of radioactive iodine by the normal and disordered thryoid gland in children 574
Hawley, P. R.: Tuberculosis program of Veterans' Administration 574
Russakoff, A. H.: Tuberculosis in Alabama state hospitals 575
Hilleboe, H. E.: Recent developments in tuberculosis control 575
Woodruff, G. E.: Quantitative tuberculin test 575
Baggenstoss, A. H., Feldman, W. H., and Hinshaw, H. C.: Streptomycin in miliary tuberculosis 575
Long, E. R.: Tuberculosis experience of United States Army in World War II 575
Siltzbach, L. E.: Carcinoma simulating pulmonary tuberculosis 576
Rigler, L. G., and Kelby, G. M.: Emphysema 576
Valle, A. R., and White, M. L., Jr.: Pulmonary tuberculosis simulating bronchogenic carcinoma 577
Birath, G.: Pulmonary function following pneumothorax 577
Ingegno, A. P., D'Albora, J. B., Edson, J. N., and Gianquinto, P. J.: Pneumonia associated with acute salmonellosis 577
Adams, J. M.: Congenital pneumonitis in newborn infants 578
Lemone, D. V., Scott, W. G., Moore, S., and Koven, A. L.: Bagasse disease of lungs 578

General

Pautrier, L. M.: Sarcoidosis 578
Haxthausen, H.: On the Kveim reaction in Boeck's disease 579
Freudenthal, W.: Sarcoid 579
Refvem, O.: I. Chronic granulomas in the alimentary tract caused by minute mineral particles. II. "Boeck's disease" and occurence of minute mineral particles 579
Bjørnstad, R. T.: Progressive Boeck's sarcoid associated with protracted destructive tuberculosis 580
Mueller, J., and Pedrazzini, A.: Besnier-Boeck disease with transition into miliary tuberculosis 580
Gardner, C. E.: Foreign body localization in the soft parts 580

ROENTGEN AND RADIUM THERAPY

Loebell, M. A.: Simultaneous cross-radiation 580
Craver, L. F.: Lymphomas and leukemias .. 581
Walker, H. J., and Schulz, M. D.: Carcinoma of the tonsil 582
Windholz, F.: Biological significance of fibrinous radiomucositis of the larynx 582
Windholz, F.: Reactions of connective tissues after protracted fractionated irradiation of laryngeal carcinoma 582
Hale, C. H., and Holmes, G. W.: Carcinoma of the skin 583
Pohle, E. A., and Morton, J. A.: Roentgen therapy in arthritis, bursitis, and allied conditions 583
MacCarty, W. C.: Effects of estrogenic therapy on osseous metastases from carcinoma of the prostate 584

MISCELLANEOUS

Gianturco, C.: Elastic ruler for roentgen pelvimetry 584
Lipp, C. S., and Smith, R.: Latex cap for radon ointment treatment 584
Vincent, J. G., Vincent, H. W., and Dowdy, A. H.: Experimental clostridial infections in dogs 584
Raper, J. R.: Effects of total surface beta irradiation 585
Tansley, K., and Wilson, C. W.: Irradiation of experimental cerebral tumours 585
Chalecke, W. E., Jones, G. E., Miller, L. L., Steinhausen, T. B., and Strain, W. H.:

Iodinated organic compounds as contrast media for radiographic diagnosis. VI. 586
George, M. P., Mahoney, E. B., Pearse, H. E., and Strain, W. H.: Iodinated organic compounds as contrast media for radiographic diagnoses. VII. 586
Jones, G. E., Chalecke, W. E., Dec, J., Schilling, J. A., Ramsey, G. H., Robertson, H. D., and Strain, W. H.: Iodinated organic compounds as contrast media for radiographic diagnosis. VIII. 586
Halberstaedter, L., and Ickowicz, M.: Early effects of x-rays on the ovaries of the rat. 586
Hamilton, J. G.: Metabolism of fission products and the heaviest elements. 587
Chamorro, A.: Biological bases of an associated action of hormones and roentgen rays on cancerous cells of certain glands under hormonal control. 588
Landauer, R. S.: Application of inverse-square law to oil-immersed tubes. 588
Trout, E. D., and Atlee, Z. J.: Low-absorption roentgen-ray measurements from 500 to 1,000 kilovolts. 588
Rogers, T. H.: High-intensity radiation from beryllium-window x-ray tubes. 589
Mallet, L., and Maurin, R.: Study of quality and origin of parasitic radiation from the target of an x-ray tube. 589
Lange, K., and Evans, R. D.: Absorption of radon through the skin and its exhalation through the lungs. 589
Jacobson, L. O., and Marks, E. K.: Hematological effects of ionizing radiations in the tolerance range. 590

ROENTGEN DIAGNOSIS

NECK AND CHEST

Olsen, Arthur M. Esophagitis. (Editorial) *Surg., Gynec. & Obst.*, March, 1948, *86*, 372–374.

Apparently esophagitis is a condition which is seldom recognized during a patient's life. Paul has stated that acute ulcerative esophagitis is a common finding at necropsy but rare in clinical practice. Vinson and Butt found that in 75 per cent of their 213 cases of esophagitis (found at necropsy) the patients had been operated upon a short time before. The disease is encountered commonly in patients who have gallbladder disease, duodenal ulcer, obstructing lesions of the gastrointestinal tract and esophageal hiatal hernias. The condition is probably the result of reflux of gastric secretions into the esophagus. The digestive juices are very irritating to the esophageal mucosa. Esophagitis is likely to occur in association with abdominal diseases that produce excessive vomiting.

The cardiac sphincter is incompetent in many cases of esophageal hiatal hernia and esophagitis frequently is associated with hiatal hernia. Many years ago Cushing called attention to the frequent occurrence of esophagitis and esophageal ulceration in patients with lesions of the brain.

The symptoms of esophagitis frequently are overlooked. Such terms as "heartburn" and "sour stomach" are often used to describe a substernal and epigastric burning sensation caused by inflammation of the lower part of the esophagus. In cases in which the disease is severe patients may complain of substernal pain, sometimes referred up to the throat and neck and even into the arms. Such pain usually indicates esophageal spasm.

In most cases esophagitis probably subsides without leaving any ill effects. However, repeated episodes of esophagitis lead to a progressive cicatrization of the lower part of the esophagus.—*Mary Frances Vastine, M.D.*

Gross, Robert E., and Neuhauser, Edward B. D. Compression of the trachea by an anomalous innominate artery; case report. *Am. J. Dis. Child.*, April, 1948, *75*, 570–574.

This report summarizes the authors' experience with the successful surgical treatment of a patient in whom the trachea was compressed by an innominate artery which lay in an unusual position. The patient was an infant girl, aged four months, with symptoms of noisy breathing, particularly during inspiration and a respiratory rate of 44 per minute. There was no cyanosis. Fluoroscopic examination showed no abnormality of the heart or lungs. The swallowing function appeared normal, and no extrinsic pressure was evident in the esophagus filled with barium sulfate. Roentgenograms of the chest showed no abnormality in the anteroposterior position, but in the lateral projection definite narrowing of the trachea could be seen. Iodized oil was instilled into the trachea for better visualization. In the anteroposterior view slight broadening of the trachea just below the

thoracic inlet could be seen. In the lateral view an extrinsic pressure defect was present on the anterior aspect of the trachea. This defect was just above the level of the aortic arch and coursed obliquely upward from left to right. It was thought that this defect was produced by an aberrant artery arising on the left side of the aortic arch and passing obliquely in front of the trachea to its distribution on the right side.

At operation the innominate artery was found to arise from the aortic arch somewhat to the left of its normally expected position, and it had a common origin with the left common carotid artery. As the innominate artery coursed to the right, upward and backward, to reach the thoracic outlet, it forcibly pressed on the right anterolateral and the anterior surfaces of the trachea in such a way as to deform it and reduce the size of the tracheal lumen. The innominate artery was anchored in a forward position by tacking it to the back of the sternum. After operation the baby had an extremely satisfactory convalescence. On the sixth postoperative day, bronchograms showed great improvement in the appearance of the trachea. The slight defect still present did not have the appearance of an indentation due to external compression and it was interpreted as representing a mild structural deformity of the trachea which had developed as a result of the external compression which had existed throughout the life of the baby prior to operation. She was seen three months after operation and was entirely asymptomatic.—*R. S. Bromer, M.D.*

EVANS, TITUS C. Preparation of radioautographs of thyroid tumors for study at high magnification. *Radiology*, August, 1947, *49*, 206–213.

In an attempt to obtain sharp autoradiographs that could be easily compared with the histologic anatomy of thyroid tumors after administration of radioactive iodine, the author mounted tissue sections directly on the photographic emulsion of a 2 by 2 inch Eastman lantern slide, medium contrast. After photographic processing, these slides were then stained by hematoxylin and eosin and the result gave a complete record of the location of the iodine and the cellular morphology simultaneously. It is felt that this is a definite improvement on the older method of making separate autoradiographs and stained tissue sections and superimposing them for study.—*Robert P. Barden, M.D.*

QUIMBY, EDITH H., and MCCUNE, DONOVAN J. Uptake of radioactive iodine by the normal and disordered thyroid gland in children. *Radiology*, August, 1947, *49*, 201–205.

Carrier-free radioactive iodine was administered to infants and children to determine its usefulness as an indication of thyroid function. Oral doses of from 20 to 40 microcuries were followed by concentration and retention in the thyroid gland of about 12 per cent in children without thyroid disease, much higher amounts in hyperthyroidism, and less than 1 per cent in hypothyroidism. In the occasional patient without thyroid disease, an extremely low uptake was encountered. The authors feel this may be explained by a high intake of iodine previous to the test, or to debilitating disease at the time of the test.—*Robert P. Barden M.D.*

HAWLEY, PAUL R. The tuberculosis program of the Veterans' Administration. *Am. Rev. Tuberc.*, Jan., 1947, *55*, 1–7.

Responsible for the largest known group of tuberculosis patients, the Veterans Administration may be expected to assume leadership in the fight against this disease. For the peak year of 1950, a need for 15,000 beds is anticipated and this requirement is being met through acquisition of Army hospitals and new construction. The present bed capacity is approximately 6,000.

The ratio of doctors to patients, including various specialists, has been set at approximately 1 to 35, and a goal has been fixed for at least one nurse to five patients.

Through a tuberculosis case-finding program, any veteran who comes to the Veterans Administration will get a chest roentgen examination if he has not had one within the past six months.

Tuberculosis patients will be treated at five types of institution. 1. Tuberculosis units within neuropsychiatric hospitals. 2. Sections of not less than 100 beds in general hospitals. 3. Convalescent rural sanatoriums for ambulant patients. 4. Isolated "health resorts" for patients with positive sputum but for whom definitive treatment is inadvisable. 5. Communities for severely handicapped but ambulant patients with negative sputum.—*J. J. McCort, M.D.*

Russakoff, A. H. Tuberculosis in the Alabama State hospitals. *Am. Rev. Tuberc.*, Jan., 1947, *55*, 93–101.

A mass roentgenographic survey of two state mental hospitals was made using 35 mm. films. Persons found to have suspicious and definite infiltrations were recalled for a conventional 14 by 17 inch film.

Including the known cases of tuberculosis prior to the time of the this study, the overall prevalence of reingestion tuberculosis is 5.0 per cent. Although the results of this study disclose the prevalence of tuberculosis to be lower than that in some other institutions for the mentally ill, the author feels that tuberculosis constituted a major public health problem among patients and employees alike in the Alabama state hospitals.—*J. J. McCort, M.D.*

Hilleboe, Herman E. Recent developments in tuberculosis control. *Am. Rev. Tuberc.*, Jan., 1947, *35*, 17–20.

Within the next five years, the Tuberculosis Control Division will continue its case finding and follow-up program and will set as its goal examination of the majority of persons over fifteen years of age in the population of the United States. Such an intensive campaign will make necessary increased efforts in providing simultaneously medical care and isolation, after-care and rehabilitation and protection of the patient's family against economic distress. Those objectives can be attained in that relatively short period. Then the stage will be set for the final eradication of tuberculosis in the United States.—*J. J. McCort, M.D.*

Woodruff, G. Eugene. The quantitative tuberculin test; its significance in the diagnosis of tuberculosis. *Am. Rev. Tuberc.*, June, 1947, *55*, 488–494.

1. The patient in relatively good general condition who is suspected of having tuberculosis should exhibit a positive tuberculin reaction in confirmation of the diagnosis.

2. In any large series of patients with roentgenograms suggestive of tuberculosis, a certain number will be encountered who fail to react to tuberculin high concentration. The differential diagnosis in such cases is simplified by the knowledge that the patient with active pulmonary tuberculosis who is anergic is always critically ill. Any anergic patient who does not appear ill is probably montuberculous, regardless of the roentgenographic findings.

3. Tubercle bacilli are never found in the sputum of an anergic patient unless he is critically ill.

4. The anergic tuberculous patient is much more likely to have large numbers of tubercle bacilli in his sputum than is the highly allergic patient.

5. Routine tuberculin tests are one of the most important contributions of the laboratory to the diagnosis of tuberculosis.—*J. J. McCort, M.D.*

Baggenstoss, Archie H., Feldman, William H., and Hinshaw, H. Corwin. Streptomycin in miliary tuberculosis: its effect on the pathological lesions of generalized miliary tuberculosis in human beings. *Am. Rev. Tuberc.*, Jan., 1947, *55*, 54–75.

Clinical, roentgenological and pathological observations concerning 5 patients who had fatal miliary tuberculosis treated with streptomycin are reported. Evidence of regression and healing of the miliary tubercles in the lungs was observed roentgenologically in 4 cases, ophthalmoscopically in the choroid layer of the eye in 2 cases and histopathologically in the lungs and liver in 4 cases and in the spleen in 3 cases. The development of widespread tuberculous meningitis apparently was inhibited in 1 case and was either prevented or cured in 2 other cases. No histopathological evidence of any toxic effect of the drug could be found with the possible exception of renal tubular damage which occurred in 1 case. These observations offer further encouraging evidence of the therapeutic efficiency of streptomycin in tuberculosis.—*J. J. McCort, M.D.*

Long, Esmond R. The tuberculosis experience of the United States Army in World War II. *Am. Rev. Tuberc.*, Jan., 1947, *55*, 28–37.

It is known, through sampling done by the Office of the Surgeon General during the war, and through comparison of induction and discharge films of men breaking down, that several thousand small infiltrative lesions were overlooked by the induction station roentgenologists in the millions of films examined. But it is a fair estimate that 90 per cent of the significant lesions that should have been seen were discovered.

Such oversights should never occur in such

number again. The best insurance against their recurrence is a well-trained, stable personnel, experienced in the detection of tuberculosis, and on duty in sufficient numbers so that no man is expected to carry a load of more than 300 films a day over prolonged periods of time. From the point of view of administrative efficiency, the author believes this personnel should be military, not civilian. It would be preferable to hold young officers in Army training stations longer and then keep them on the job. Substitution of tuberculosis experts trained in reading chest films only, as from time to time suggested, would not solve the problem. Chest lesions of incredible variety are seen in induction stations and one-fifth of the films taken are of other parts than the chest.

The Army does not consider the long range care of tuberculosis a proper responsibility of the Army Medical Corps. Tuberculosis requires long treatment, and, as far as possible, that care should not be broken up. It should proceed in an orderly manner in one sanatorium, with proper convalescent follow-up and modern rehabilitation measures. The system of Veterans hospitals has been set up for this purpose.—*J. J. McCort, M.D.*

Siltzbach, Louis E. Carcinoma simulating pulmonary tuberculosis. *Am. Rev. Tuberc.*, Feb., 1947, *55*, 170–176.

The author reports on 2 cases which were treated for pulmonary tuberculosis for periods of seven and sixteen months, respectively, before the neoplastic nature of the lesions was recognized. A proper evaluation of the alterations in the appearance of the lesion on successive films was crucial in both these cases, since neither of the patients had any symptoms for the many months of observation prior to surgery.

The progression of the lesions on the roentgen film in these 2 cases may be summed up as follows: Initially, both lesions measured about 2 cm. and had a veil-like, somewhat amorphous appearance, but on close inspection it could be seen that the mesial borders were rounded where as the lateral borders faded out and were streaky. These streaked shadows probably represented small foci of atelectasis arising either from obliteration of small bronchial lumina by the neoplasm or from pressure exerted upon the lumen by the expanding extramural mass.

Later, the shadow became denser and more sharply demarcated from the surrounding lung parenchyma and it then represented the neoplasm itself. A distinguishing roentgen feature in the second case was central necrosis of the neoplasm, which was suggested by the presence of several small irregular areas of lesser density within the solid shadow. The author states that should such areas be visible within the mass on the initial film and should the sputum be persistently free of tubercle bacilli, such a lesion must be preserved to be neoplastic and exploratory operation is warranted.—*J. J. McCort, M.D.*

Rigler, Leo G., and Kelby, Gjert M. Emphysema; an early roentgen sign of bronchogenic carcinoma. *Radiology*, November, 1947, *49*, 578–586.

The authors report 5 cases in detail and mention 2 additional cases in which obstructive emphysema was an early manifestation of bronchogenic carcinoma. According to Westermark the effects of bronchostenosis may be divided into the following four stages: 1. Diminution of aeration as the result of minimal stenosis. Cases in this stage are difficult to detect roentgenologically. 2. The stenosis becomes of higher grade. Air can enter during inspiration but due to diminution in the size of the bronchial lumen during expiration it is much more difficult for it to escape. This results in relative emphysema of the abnormal lung, which may not be evident in a roentgenogram made in inspiration but which can be readily detected under the fluoroscope or in a film made in expiration. 3. As the stenosis increases there will come a stage when there is inspiratory as well as expiratory emphysema. 4. When the tumor with its debris or inflammatory products completely occludes the bronchus, atelectasis results.

As the only hope of curing bronchogenic carcinoma is early diagnosis, careful study should be given to minor differences in radiability of the two lungs to determine whether obstructive emphysema is present. Such a finding should lead to further investigation by bronchography, planigraphy, and bronchoscopy. Patients suspected of bronchogenic carcinoma but without frank roentgen findings should always be examined in expiration as well as inspiration.—*Arthur E. Childe, M.D.*

Valle, Anibal Roberto, and White, M. Lawrence, Jr. Pulmonary tuberculosis simulating bronchogenic carcinoma; report of four cases. *Am. Rev. Tuberc.*, May, 1947, *55*, 449–456.

In spite of modern methods, differential diagnosis is often difficult in these cases without exploration. In this series, cough, gradually becoming productive, small hemoptysis, chest pain, weight loss, and weakness were all symptoms common to bronchogenic carcinoma and tuberculosis or other chronic inflammatory disease. In 3 cases of this series orthodox methods, carefully and repeatedly applied, failed to reveal tuberculosis, in spite of active lesions, both clinically and pathologically. In the fourth case pathological inactivity of the lesion makes the negative studies less surprising. The roentgen picture in all cases was suggestive of carcinoma and the bronchoscopic examinations were noncontributory.

The authors summarize by stating that diagnostic mistakes revealed only at or after operation must be accepted if we are to make an effective attack on cancer of the lung. They can be excused only if conscientious and complete attempts at ruling out tuberculosis have been carried out.—*J. J. McCort, M. D.*

Birath, Gösta. Pulmonary function following pneumothorax. *Am. Rev. Tuberc.*, April, 1947, *55*, 349–365.

Twenty-five patients with pleurisy with effusion without parenchymal lesions, and in whom so-called preventive pneumothorax treatment had been terminated, were examined by the author's method for the estimation of the total lung volume and its subdivisions and of the respiratory dead space.

The following results were obtained:

1. Total and vital capacities were diminished.
2. Equilibrium and residual capacities were not generally diminished to the same degree.
3. While the diminished total and vital capacities were due to the impairment of the thoracic and diaphragmatic mobility through pleural adhesions the cause of the increased relative lung volume values was a hypoventilation of certain parts of the lung, provoked by the same cause. In 11 cases of terminated pneumothorax treatment chosen to throw light on the subject, and with more or less extensive parenchymal lesions, the following was found.
4. The lung function, in several cases, was seriously impaired, manifesting itself in low total and vital capacities, considerable increase of the relative lung-volume values and in certain cases increased values for the respiratory dead space.
5. The cause of this was, in some cases, in part parenchymal contraction with so-called compensatory emphysema and reduction of the parenchyma, but in the majority of cases the cause was pleural changes following pneumothorax treatment (venilatory insufficiency).
6. In view of the very serious impairment of function that may result when a lung retraction complicates pneumothorax treatment, it is suggested that in certain cases this treatment should be abandoned and replaced with other collapse measures.—*J. J. McCort, M.D.*

Ingegno, Alfred P., D'Albora, John B., Edson, John N., and Gianquinto, Peter J. Pneumonia associated with acute salmonellosis. *Arch. Int. Med.*, April, 1948, *81*, 476–484.

In an outbreak of acute salmonellosis, due to *Salmonella montevideo*, 19 patients had evidence of bronchopulmonary involvement. Four had acute bronchitis. One patient had definite bronchopneumonia with sputum which contained the *Salmonella* organism. The other 14 patients had interstitial pneumonia. The pathogenesis of the interstitial type is unknown, but the clinical and roentgenologic features suggest a virus origin.

Roentgenologic examinations of the chest show changes interpreted as indicative of interstitial pneumonia in all patients. In 8 the changes were bilateral, while in 6 the right side only was affected. These interstitial changes were patchy or diffuse and in 2 instances were accompanied with partial consolidation. In 1 patient there was evidence of pleuritis at the base of the right lung. Resolution began within four to seven days of onset and in almost all was completed in about two weeks. There was neither clinical nor roentgenologic evidence of any suppurative complication.

A scattering of other symptoms and signs include asthenia, general malaise, anorexia, herpes labialis, chills, aches and pains, neuritic pains and dysesthesias, sweats and transient urticaria.

It may be assumed that true *Salmonella* bronchopneumonia with pulmonary consolida-

tion is probably a relatively rare manifestation of salmonellosis. Diagnosis is established by demonstration of the causative organism in the sputum or puncture of the lung.—*Eugene J. McDonald, M.D.*

Adams, John M. Congenital pneumonitis in newborn infants. *Am. J. Dis. Child.*, April, 1948, *75*, 544–554.

A relation between infections of the upper respiratory tract in mothers and primary pneumonitis in their infants is considered likely by the author. He suggests that the same causative factor may be involved and that this agent may be responsible for pathologic changes in the pharyngeal epithelial cells of both the mother and her baby. These changes are represented by large numbers of typical cytoplasmic inclusion bodies seen in the pharyngeal epithelium of both mother and the baby and in the alveolar and bronchial epithelium of the infants who die of pneumonitis.

Reports of 6 cases of congenital infections of the respiratory tract are given, together with a brief review of the pertinent features of primary virus pneumonitis with therapeutic suggestions. Roentgenograms of the chest in several of the cases showed slight infiltration, a soft diffuse shadow in the lungs, in the right upper and lower lobes and in others there was a distinct increase in the bronchovascular markings in both lungs. The disease in the newborn and young infants is characterized clinically by an acute onset of sneezing, coughing, dyspnea and cyanosis. The elevation in temperature was moderate to low, some infants showing no elevation. The mortality was definitely correlated with the severity of symptoms and signs.—*R. S. Bromer, M.D.*

Lemone, David V., Scott, Wendell G., Moore, Sherwood, and Koven, A. Link. Bagasse disease of the lungs. *Radiology*, November, 1947, *49*, 556–567.

Bagasse is the name given to sugar cane after it has been crushed and the juice extracted. Bagasse disease of the lungs, or bagassosis, is a pulmonary disorder brought about by the inhalation of dried bagasse dust.

Bagasse fibers are tough and possess insulating qualities. Bagasse is being used more extensively in the manufacture of thermal and noise-insulating building materials and in the manufacture of refractory brick. Unless properly handled, it constitutes a serious industrial hazard. About 40 cases of bagassosis have been reported in workers in sugar cane processing plants, and in plants where the bagasse is manufactured into building boards or refractory brick.

The symptoms and clinical course of bagassosis are variable, depending on the length of exposure and the density of the inhaled dust. In general, about two months of exposure to the dust are required before symptoms appear. Onset is insidious, the patient usually not realizing that he is ill until he is seized by a sudden coughing spell and extreme dyspnea. An acute febrile illness follows, or acute bronchiolitis. In lighter cases of briefer exposure, the disease clears up in two to six months. Patients with long exposure are critically ill. An 8.3 per cent mortality rate has been reported in one series.

Eosinophilia is usually present. Roentgenographically, a diffuse fine punctate infiltration is seen, which tends towards a nodular appearance as the disease starts to clear up. Areas of consolidation may be present, especially in and near the hilum. The roentgen findings are not diagnostic, but the reversibility of the process distinguishes it from the other pneumoconioses.

The exact etiology of the disease is obscure and there is no specific treatment. No response to chemotherapy has been observed. Oxygen affords some relief from the dyspnea in the more severe cases. The authors report 3 cases in detail.—*George Cooper, Jr., M.D.*

GENERAL

Pautrier, L. M. Sarcoidosis. *Brit. J. Tuberc.*, January, 1948, *42*, 1–7.

The author discusses two prevalent theories of the etiology of sarcoidosis: namely, the concept of a tuberculous origin and the belief of an indeterminate virus as a cause. To refute the first the author points out that the histopathological picture of sarcoid is not characteristic of tuberculosis; no tubercle bacilli are found in lesions of sarcoid; and the tuberculin test is usually negative. He dismisses the belief that sarcoid is genuine tuberculosis modified by special reactions on the part of the organism. He analyzes the evidence with respect to the second theory and finds little support for it. The reliability of the Kveim reaction, which has been advanced as proof for such a belief, has been questioned by some investigators.

The writer feels that sarcoidosis is clinically an autonomous disease and not a single monomorphic tissue reaction produced by various agents. He concludes that the etiology remains unsettled.—*Harry L. Berman, M.D.*

Haxthausen, H. On the Kveim reaction in Boeck's disease. *Brit. J. Tuberc.*, January, 1948, *42*, 7–11.

The author discusses the role of the Kveim reaction in attempting to decide whether sarcoid is a form of tuberculosis or a disease per se. The Kveim test consists of the intradermal injection of a suspension of granulation tissue characteristic of the disease. The reaction appears after a latent period of one to two weeks or longer and consists of a papule increasing in size to a small nodule and disappearing in several months to two years. The test has been considered to be positive "nearly always" in sarcoid and negative in other diseases. The pathogenesis of the reaction is not entirely clear. Some features suggest an isomorphic reaction; that is, the local reproduction in the skin of a lesion found elsewhere in the body. Other features suggest a specific allergic reaction. The author emphasizes the need for further study and concludes that the Kveim reaction has not settled the controversial aspects of the nature of sarcoid.—*Harry L. Berman, M.D.*

Freudenthal, W. Sarcoid. *Brit. J. Tuberc.*, January, 1948, *42*, 11–16.

In analyzing the chief features of sarcoid which are considered to be proof against the tuberculous etiology of the disease—namely, the histopathological picture, the negative tuberculin reaction, and the absence of tubercle bacilli in the lesions—the author presents evidence showing that these arguments are not entirely correct. He demonstrates typical Langhans' giant cells in some cases of sarcoid, distinct inflammatory components in others, and sarcoid-like pictures in cases of lupus muliaris facei. He calls attention to the fact that positive tuberculin tests are changed to negative during the course of certain infectious diseases and are modified by prior injections of BCG vaccine and tuberculin. As regards the presence of tubercle bacilli, it is claimed that positive cultures are being obtained. Furthermore, the bacilli are seldom found in lesions of the tuberculous dermatoses. The author states that the problem of the nature of sarcoid is still unsolved but that the findings described above are compatible with a tuberculous etiology.—*Harry L. Berman, M.D.*

Refvem, Olav. I. Chronic granulomas in the alimentary tract caused by minute mineral particles. II. "Boeck's disease" and occurrence of minute mineral particles. *Acta path. et microbiol. Scandinav.*, January–February, 1948, *25*, 107–121.

A series of conditions in the alimentary tract, such as gastric or intestinal cellulitis, regional enteritis, anal abscess or anal fistula, have been regarded as foreign body reactions, isolated or combined with a bacterial infection. The presumptive foreign body etiology in these cases is supported by few observations and mainly by theoretical deductions. For this study the polarization microscope was used systematically in a series of cases. It was used chiefly to detect cholesterol crystals. Frequently oil droplets, mucous material, hairs, talcum particles were found. In animal experiments silica was injected and often produced a picture resembling the histopathological manifestation of tuberculosis.

Where the foreign bodies are few and very small, the differentiation from smudge may be very difficult. To be accepted as a causative agent, the particles must be situated exactly in the same plane as that of the tissue and naturally embedded in the pathological tissue. The main problem to decide, when foreign material is found, is whether its presence can explain the whole or part of the clinical picture. Foreign bodies were found in about 25 per cent of 209 cases examined. In the anorectal region 34 per cent showed foreign bodies and 75 per cent of these cases showed talc foreign bodies. About two-thirds of talc fistulas in the anal region occurred in men.

II. Histological sections from 100 cases diagnosed as Boeck's disease were examined in polarized light, each case represented by biopsy from one or several lesions. Most of the various sections when examined by polarized light almost always showed a foreign body granuloma embedded in giant cells. The author stresses the possibility of foreign bodies being one of the causes of Boeck's disease. He believes the remissions may be due to a breakdown and disappearence of certain foreign bodies in the tissues.—*Robert J. Reeves, M.D.*

Bjørnstad, Roar Th. Progressive Boeck's sarcoid associated with protracted destructive tuberculosis. *Acta tuberc. Scandinav.*, 1948, *22*, 143–153.

The coincidence of Boeck's sarcoid and tuberculosis is a rather infrequent occurrence, considering the high incidence of tuberculosis alone. Every eighth individual in Norway dies of tuberculosis. One case is reported showing no regression of the sarcoid manifestations in spite of the patient having a protracted, destructive tuberculosis. The tuberculous and sarcoid manifestations did not seem to have any mutual influence upon each other. Reports are given of cases showing regression of sarcoid lesions in connection with the development of a tuberculous process. On studying different papers by the author, one is not convinced that there is a spontaneous regression of sarcoid as the tuberculosis develops but that this may be more of a coincidence.—*Robert J. Reeves, M.D.*

Mueller, J., and Pedrazzini, A. Morbus Besnier-Boeck mit Übergang in Miliartuberkulose. (Besnier-Boeck disease with transition into miliary tuberculosis.) *Schweiz. med. Wchnschr.*, February, 1948, *78*, 126–128.

This is a case report of a twenty-seven year old patient in whom the diagnosis of Boeck's disease was made in 1937 on the basis of hilar lymphadenopathy. His general condition remained good and the local pathology stationary for ten years. Tuberculin reactions were essentially negative during the same period. His terminal illness started with spiking elevations of temperature, acute and profound malaise, rapidly leading to his death. A roentgenogram of his chest revealed miliary dissemination. Also the tuberculin reaction had now become positive in a dilution of 1:100,000. Postmortem examination revealed miliary tuberculosis and hyalin-nodular changes of the paratracheal and paraesophageal lymph nodes as seen in Boeck's disease.—*A. Grishman, M.D.*

Gardner, Clarence E. Foreign body localization in the soft parts; a simple method requiring no especial training or equipment. *Surgery*, February, 1948, *23*, 275–277.

The author reports that Reed and Black, in a review of the literature in 1938, classified the methods of localization of foreign bodies under ten different principles. The method used in 110 cases was reported. It consists of the insertion, under roentgenoscopic control, of two long slender needles. They are inserted at right angles into the tissue at a distance from the proposed incision so that they cross in the approximate location of the foreign body. Anteroposterior and lateral views then are exposed and, with the needle still in place, the field is draped and the area explored at operation.—*Frank H. Marek, M.D.*

ROENTGEN AND RADIUM THERAPY

Loebell, M. A. Simultaneous cross-radiation. *Radiology*, June, 1947, *48*, 570–578.

In February, 1938, in a paper written by the author the advantages of simultaneous cross radiation were discussed and a description was given of apparatus built for that specific purpose. The original model was improved, the present apparatus consisting of a shock proof, oil-filled, lead-lined steel tank containing a 200 kv. transformer surrounded by 4 balanced roentgen-ray tubes. Changing the position of the openings in the regulating diaphragm makes possible the dovetailing of roentgen-ray beams which may be concentrated on a tumor with little cross radiation outside of the neoplasm. Targets are arranged at 60° angles. A series of heavy lead diaphragms, encased in sheet steel, each of which has four apertures, is calculated to allow the roentgen-ray beams to cross at different depth levels of 1 cm. variations below the surface of the skin. The relative position of the openings in the diaphragms determines the level of cross radiation. On each diaphragm is indicated the thickness and kind of filter and the exact target-skin distance. Because of the variation in the size of roentgen-ray beams at different levels apertures in the several diaphragms differ slightly in size, so that the area of cross radiation in the present model is exactly 100 sq. cm. at all levels.

Theoretically, the ideal method of irradiating a tumor would be to give a saturation dose and then repeated smaller doses at frequent intervals, keeping the saturation point constant during the entire cycle of malignant cell mitosis. In deep-seated tumors the danger to adjacent healthy tissues constitutes an obstacle. This difficulty is solved in part by changing the position of the patient, or the course of entry, or both, in such a manner that the roentgen-ray beams cross their own path at a certain depth

below the skin, producing a radiation effect of greater intensity at the tumor depth, and distributing the superficial dose over a larger area. Simultaneous cross radiation is based on the principle of administering quickly large doses of radation at depth and distributing the superficial dose over large areas through a great number of ports at the same time. The advantage lies in the fact that a carcinocidal dose can be administered to a neoplasm, while the tumor bed, receiving a non-lethal dose, recovers quickly and is capable of replacing destroyed malignant structures with benign fibrous tissue, blood vessels and the like. Large daily doses applied directly to a neoplasm tend to keep the saturation point constant and the result compares favorably with that obtained in superficial therapy. A carcinocidal dose can be administered with simultaneous radiation at any depth. This is made possible by the great number of ports of entry (32 or more) through which roentgen-ray beams are brought to converge on any specific area, producing a homogeneous radiation effect.

Eleven case reports are given. In a boy of three years an osteolytic tumor involving the right sacroiliac junction was shown on biopsy to be due to a sarcoma. The boy was treated by the multiple port method for a total tumor dose of 2,146 roentgens. Six years later the child appeared well without any sign of recurrence.—*Samuel G. Henderson, M.D.*

Craver, Lloyd F. Lymphomas and leukemias. *J.A.M.A.*, Jan. 24, 1948, *136*, 244–248.

In spite of the fact that it is doubtful if anyone is in a position to authenticate a claim to have cured any case of Hodgkin's disease, lymphosarcoma, mycosis fungoides or leukemia up to the present time, early diagnosis and treatment of these diseases affords better results in terms of long control. Hodgkin's disease and lymphosarcoma of unicentric origin offers the possibility of cure or eradication by complete surgical excision, heavy regional irradiation, or a combination of both when the disease is confined to one organ or nodal mass. Lymphosarcoma in certain regions such as the head and neck may show a postoperative survival which is double the rate for lymphosarcoma of all types. Surgical survivals seem to exceed irradiation survivals of those with localized lesions, although the groups are not clinically comparable.

For chronic leukemia, a great deal can be accomplished in a palliative way by judicious irradiation even though one must accept incurability as the first premise. Early diagnosis cannot wait for the development of typical textbook symptoms and signs. Early biopsies of Hodgkin's disease and lymphosarcoma frequently fail to reveal the diagnosis and early blood counts may not reveal leukemia.

It is urged that enlarged lymph nodes be investigated for cause and biopsied if no primary lesion is found. Biopsy of more than one node is often advisable. Unicentric lymphomas may be disguised as solitary nodules in the thyroid, breast, base of the neck between the sternocleidomastoid muscle insertions, tonsil, mediastinum, skin, orbit and lacrimal gland, and as a reticulum cell sarocma of bone. Chronic lymphatic leukemia may produce as its first manifestation local tumors reported on biopsy as lymphosarcoma. The use of sternal puncture to detect early lymphatic and myeloid leukemias is important. Osteosclerotic anemias mimic myeloid leukemia by producing compensatory splenic enlargement.

Prevention of these diseases may be gained in some measure by control of exposure to benzene solvents, radioactive emanations, sulfonamide drugs in children, chronic infections, atypical variants for tuberculosis, allergies, heredity, and endocrine dyscrasias. No attempt is made to formulate any set of rules for prevention of these diseases.

Treatment of lymphomas and leukemia by nitrogen mustard, radioactive isotopes, and urethane affords only palliative results. It is clear that these toxic constitutional agents have little or no place in the treatment of early localized Hodgkin's disease or lymphosarcoma. For such cases adequate local roentgen therapy remains the treatment of choice, except perhaps in those cases that lend themselves to radical surgical procedures, which should probably be followed by moderately heavy local postoperative roentgen therapy. Adequate roentgen-ray dosage should be far more than just enough to cause regression. Fractional dosage to skin tolerance is recommended for local areas. Total body irradiation following local irradiation will unpredictably confer longer freedom from relapse in Hodgkin's disease and lymphosarcoma. Doses of 75 to 125 r, in air, are used. Myeloid leukemia responds best to splenic irradiation in daily fractions. Lymphatic leuke-

mia with splenohepatomegaly, enlarged peripheral nodes and bone marrow changes may derive benefit from 200 r to 300 r once around each of the external lymph node bearing areas. It is recalled that some cases of lymphatic leukemia show no enlarged lymph nodes, and some myeloid leukemias do not have splenic enlargement.—*J. A. Campbell, M.D.*

WALKER, H. JOHN, and SCHULZ, MILFORD D. Carcinoma of the tonsil; a review and its results in a group of ninety cases. *Radiology*, August, 1947, *49*, 162–168.

This is a study of 90 cases of carcinoma of the tonsil seen at the Collis P. Huntington Memorial Hospital from 1936 through 1941, and Massachusetts General Hospital from 1936 through 1945.

Histopathologically this group of tonsillar carcinomas were, in the majority of instances, of a high grade of malignancy, and approximately 90 per cent of them were squamous cell in type. The remaining 10 per cent consisted of lymphoepitheliomas, transitional cell carcinomas, and sarcomas.

It is of importance that 60 per cent of these cases presented themselves with cervical metastases when first seen and that in two-thirds of this group the "lump in the neck" was the first subjective complaint of the paitent.

Methods and types of radiation treatment used varied with the individual case. The authors stress the necessity of varying the treatment to the needs of the individual cases rather than stereotyped plan of treatment for all cases. Fifty patients were treated with supervoltage (1,000 kv. at the Huntington Hospital, and 1,200 kv. at the Massachusetts General Hospital) and 45 patients were treated with 200 kv. Total dose in the series treated with supervoltage varied from 2,400 to 6,600 r, measured in air, through a single lateral portal, the optimum dose being considered 6,000 r, the total dose with high voltage being 3,000 to 4,000 r to each of two opposing portals, measured in air. Some cases were given additional treatment, 2,500 to 3,000 r, through an intraoral cone. A few cases were also treated with interstitial radium in conjunction with roentgen roentgen therapy, both to primary tumor and metastatic cervical nodes. Neck dissection was not employed in any of the 90 cases.

The five year survival group in the entire series was 15 per cent. This survival rate compares favorably with other large series published in recent years. The authors, in comparing their results with other published studies on carcinoma of the tonsil where various forms of therapy have been used, telecurietherapy, interstitial irradiation, neck dissection, electrocautery, postulate the query as to whether any single procedure, or even several procedures can offer increased life expectancy to the patient with malignant tonsillar tumor beyond that afforded by roentgen irradiation alone. The authors do not make any definite statement as to apparent improved survival rate in those patients treated with irradiation produced with supervoltage equipment.—*E. A. Addington, M.D.*

WINDHOLZ, FRANK. The biological significance of fibrinous radiomucositis of the larynx. *Radiology*, February, 1947, *48*, 157–160.

The author comments that previous writers have pointed out that the appearance of an extensive and confluent radiomucositis indicates that the dose necessary to destroy tumor cells has been reached. In the author's experience both clinically and by study of microscopic sections, he has found that delay or absence of radiomucositis with standard dosage techniques does not necessarily mean that the cancer is not radiosensitive. He states that it merely signifies the inability or diminished ability of the connective tissue to produce fibrin. He also states that the early appearance of irradiation mucositis holds promise that a cure will be obtained. The author also stresses the interrelationship of the appearance of radiomucositis with the reactions of the connective tissue to radiant energy. He concludes, therefore, that radiomucositis is indicative of the degree and extent of connective tissue reaction and that the more marked and earlier the connective tissue reaction is, the more chances for the success of radiation therapy.—*Moris Horwitz, M.D.*

WINDHOLZ, FRANK. Reactions of connective tissues after protracted fractionated irradiation of laryngeal carcinoma. *Radiology*, February, 1947, *48*, 148–156.

While much attention has been given in the past to the radiopathology of the mucosa following protracted fractionated irradiation of laryngeal carcinoma, little has been written concerning the changes occurring in the con-

nective tissues following such irradiation. The author has beautifully demonstrated the changes appearing clinically and microscopically in the connective tissue following various doses of protracted and fractionated radiation. The author shows that the changes in the connective tissue are marked and extensive and appear both early and late in the course of the radiation administered. He also stresses the fact that when such radiation is given without fractionation the connective tissue changes which are seen to occur are irreversible and much more advanced. After protracted fractionated irradiation there are definite reversible changes noted with healing of the affected areas. These changes have also been demonstrated by the author in animal experiments.

The author divided the reactions occurring in the connective tissue following protracted fractionated irradiation into three periods: The first is a bionegative, retrogressive period characterized by exudation of fibrin, loss of nuclear staining, and frequent changes in the microchemical reaction of subepithelial collagenous fibers. This period appears coincidental with the fibrinous radiomucositis and disintegration of the epithelial cells of the mucous membrane. The author refers to the second period as that of the "biopositive regenerated period." In this period the connective tissue appears to fill out the spaces remaining after disintegration of the tumor. The fibrinoid necrotic collagen of the lamina propria is replaced by hyaline sclerotic layers. The author states that myogenous giant cells indicate the regenerative tendencies of these tissues. The inflammatory reaction of the newly regenerated connective tissue is markedly reduced and is said to be a specific effect of radiation on this structure. This has been shown by animal experiments, as well as in human tissue. The endothelium of damaged blood vessels during this period discloses obliterative changes with connective tissue proliferation. The author refers to the third period as "retrogressive" period, and this is said to occur in those cases which have been improperly irradiated or in which there has been marked sensitivity of the individual connective tissue. In these cases the newly formed connective tissues become necrotic and the mucous membrane discloses ulcerations with secondary infection which infiltrate the deeper layers of the irradiated larynx.—*Moris Horwitz, M.D.*

Hale, Clayton H., and Holmes, George W. Carcinoma of the skin; influence of dosage on the success of treatment. *Radiology*, June, 1947, *48*, 563–569.

Results were compared in the treatment of approximately 1,500 carcinomas of the skin on 1,300 consecutive patients (excluding lesions of the mucocutaneous junction) treated at the Massachusetts General Hospital during the period 1930–1944, with a view toward establishing the relation of particular dosages to success or failure of treatment and determining therefrom an optimal radiation dose.

Three hundred and eighty-seven lesions were treated surgically and 1,035 by roentgen irradiation. All the cases were followed from one to five or more years. The dosages varied from 1,200 to 6,000 r, measured in air. In 89 per cent of the irradiated cases, treatment was given in a single dose while in the remainder of the cases it was fractionated over a period of one to three weeks. Results are plotted in percentage of failures against average total dosages for single massive and fractionated treatments and the expectancies of tumor control in the various dosage ranges employed, are tabulated and discussed.

The studies indicated that 3,200 r to 3,600 r would be required by fractionation over one week to produce the same results as obtained by 1,900 r to 2,200 r by the massive single dose method.

The dose 4,500 r delivered in multiple treatments within one week, or its biological equivalent of 2,700 r by the single dose method, was suggested as an optimal dose to be delivered to a carcinoma of the skin.

Tables and discussions correlate the percentages of failures with the (1) various dosage ranges for the one week fractionation method, (2) different physical modalities for the single massive and fractionated techniques, (3) surgical as against roentgen treatment, (4) sizes of the lesions and (5) time interval between treatment and breakdown.—*E. D. Hudack, M.D.*

Pohle, Ernst A., and Morton, James A. Roentgen therapy in arthritis, bursitis, and allied conditions. *Radiology*, July, 1947, *49*, 19–25.

Roentgen therapy has been used for years in arthritis. One hundred heterogeneous cases were treated and 92 followed. Treatment was given with 400 kv. and 200 kv. Three doses of

150 r or 200 r were given. Forty per cent had two series. Seventy-five per cent of the patients reported moderate to complete relief. Placebos were not used. Harmful effects did occur occasionally. In bursitis 84 per cent received complete or satisfactory relief. Acute cases stand best chance of relief. Conclusion is made that the value is in analgesic effect.—*E. C. Baker, M.D.*

MacCarty, William C. Effects of estrogenic therapy on osseous metastases from carcinoma of the prostate. *Radiology*, July, 1947, *49*, 54–61.

The author reports on the estrogenic treatment of 29 patients showing osseous metastases from carcinoma of the prostate gland. Six were treated by orchiectomy alone, 21 by orchiectomy and stilbestrol, and 2 by stilbestrol alone.

In 10 cases the osseous metastases were thought to be favorably influenced, and in 5 of these there was definite improvement.

The metastases completely disappeared in 2 instances. In 1 of these cases there was complete recalcification of the metastatic area nineteen months after orchiectomy as the sole treatment. The second patient had had carcinoma of the prostrate gland for eight years. Roentgen therapy to the pelvis had been given with temporary improvement. Recurring metastatic lesions in the lumbar vertebrae completely disappeared eighteen months after orchiectomy and subsequent stilbestrol therapy; there had been no recurrence thirty-four months after orchiectomy, eleven years after the original diagnosis.

In 5 cases the osseous metastases became more dense and discrete. In 1 instance the metastases disappeared, only to recur with extensive osteoblastic metastases of a different type from those originally seen.

The author makes the point that the radiologist must be familiar with alterations in bone lesions produced by estrogenic therapy.—*Arthur A. Brewer, M.D.*

MISCELLANEOUS

Gianturco, Cesare. Elastic ruler for roentgen pelvimetry. *Radiology*, July, 1947, *49*, 95–96.

The author describes a correction measuring device consisting essentially of a rubber band upon which a centimeter scale has been marked. Stretching of the band produces distortion of the scale. Scales of known distortion permit determination of the degree of stretching of the band necessary to provide the proper correction for various levels in the bony pelvis. Subsequent films must be made at the same tube-film distance as used in making the distorted scales. The author claims the measurements are "quite as accurate" as those obtained by other methods.—*Chauncey N. Borman, M.D.*

Lipp, Charles S., and Smith, Rector. Latex cap for radon ointment treatment. *Radiology*, February, 1947, *48*, 161–163.

The authors describe the need for, and the preparation of a latex cap for radon ointment treatment. The method described is fairly simple and has wide application, especially in areas requiring the application of radon about the head and neck and in other small surface areas of the body. An advantage also mentioned is the fact that the latex cap may be used over and over again after being cleaned and sterilized.—*Moris Horwitz, M.D.*

Vincent, James G., Vincent, Helen Whitgrove, and Dowdy, Andrew H. Experimental clostridial infections in dogs. *Radiology*, June, 1947, *48*, 610–627.

The authors experimented with prophylactic and therapeutic measures on experimentally induced clostridial infections in dogs. The experiments included both pure strain organisms and mixtures of the various clostridia and *Staphylococcus aureus haemolyticus*. The prophylactic and therapeutic agents used were as follows: (1) roentgen ray, (2) oxygen gas, (3) oxygen gas and roentgen ray, (4) sulfadiazine, (5) sulfanilamide, (6) butyryl sulfanilamide, (7) sulfathiazole, (8) penicillin, (9) pentavalent antitoxin, (10) toxoid. Prophylactically sulfadiazine was found the most effective sulfanamid employed, although it was valueless against *Cl. oedematiens*. Therapeutically sulfadiazine was far from routinely effective. Early penicillin therapy in massive doses gave better results. When administered in small doses or late in the development of the disease this agent was not very effective.

Polyvalent antitoxin in massive doses administered rapidly was useful as late as twelve hours after inoculation. Smaller doses over a longer period of administration were relatively ineffective. Combined penicillin and antitoxin therapy gave the best results. In order to

minimize residual cardiac damage, early and adequate antitoxin therapy appears indicated.

Cl. welchii toxoid immunization protected dogs against a pure strain of *Cl. welchii*.

In the discussion Dr. Robert P. Barden emphasized the importance of the initial cleansing of the wound, the immediate bandaging and the sanitary care which the wound received. In human battle casualties the sulfa drugs, penicillin, antitoxin and early surgery are all important therapeutically. Dr. Barden is convinced that roentgen therapy is of no value. Dr. James F. Kelly took exactly the opposite stand and illustrated his point with clinical material. Dr. Dowdy, in closing, indicated that roentgen therapy is of some value but is not to be preferred over antitoxin and penicillin. In the future active human immunization will probably be possible.—*Oliver P. Winslow, Jr., M.D.*

Raper, John R. Effects of total surface beta irradiation. *Radiology*, September, 1947, *49*, 314–324.

This research was carried out at Clinton Laboratories, Oak Ridge, Tennessee, under the Manhattan Project. In order to study the effect of energy absorption distribution on biological effect, laboratory animals including mice, rats, guinea pigs, rabbits, and one-day-old baby rats were exposed in sufficient numbers to establish the pattern effects in each species. The animals were placed in plastic boxes lined with panels of phosphorus^{32} bakelite so that the animal received an equal dosage of beta rays over its entire surface. Gross effects, and the time of their appearance after irradiation, were noted. Effects such as inflammation of the eyes, eyes watery and/or sealed shut, epilation around the eyes and snout, erythema on feet and ears, hyperemia and subsequent drying of the ear tips, severe epilation, local desquamation, and ulceration were noted in relation to the time of exposure. The effects of beta irradiation varied with each species so that an acute lethal action occurred at a characteristic dosage. The main wave of mortality occurs at a somewhat later postirradiation time than following irradiation with roentgen rays or gamma rays and for lethal studies with beta rays forty-five days has been arbitrarily chosen to define a survivor in contrast to twenty-one days' survival commonly used for roentgen rays and gamma rays. The lethal action of beta rays must necessarily be brought about differently than that induced by penetrating radiations since all the energy of beta rays is absorbed in a superficial layer of tissue whose mass is small relative to the total mass of the animal. It follows then that the total energy absorbed to produce 50 per cent killing is directly proportional to the weight of the animal. The median lethal dose for each species, or the dose required to kill 50 per cent of the animals within forty-five days (beta rays) and twenty-one days (gamma rays) after exposure was found to be as follows: Baby rats were the most susceptible, the dose required being 2,200 beta rep or 510 gamma r. Rabbits were the most resistant, the dose required being 1,700 beta rep or 1,500 gamma r.

A series of experiments were performed with mice to determine the rate and pattern of recovery from total surface beta irradiation. It was found that by the split-dose technique, the recovery is at first very rapid with two-thirds of the effectiveness of the conditioning dose having been lost at the end of the third day and complete recovery having been attained by the end of the eighth day. There was also found to be an, as yet unexplained, over-recovery so that after the eighth day it required more than the standard test dose (4,700 rep) to kill 50 per cent of the animals in forty-five days. It was also found that single sublethal total surface doses of beta rays induced the formation of tumors in significant incidence in mice and rats, but produced none in either guinea pigs or rabbits.—*Robert K. Arbuckle, M.D.*

Tansley, Katharine, and Wilson, C. W. Irradiation of experimental cerebral tumors. *Radiology*, July, 1947, *49*, 62–71.

The authors produced experimental tumors in mice, both sarcomata and gliomata, by the introduction of methycholanthrene powder into the brain. Tumors were preserved by grafting pieces of their tissue into the brains of other young mice.

The brains of 39 mice were irradiated. All had gliomata grafted from the same original tumor. The half-value layer of radiation was 0.95 mm. Cu. The distance from focus spot to center of the mouse brain was 25 cm. Doses ranged from 1,623 r to 3,247 r. The mean dose rate was 154 r/min.

The effect of irradiation on the growth of the tumors was quite variable. In some the largest dose had no effect, while in others the tumor

decreased in size or disappeared temporarily. In no case was the tumor entirely destroyed. The *average* result (as measured either by the survival time or by the number of animals showing regression of the tumor) was at least as good with 2,434 r as with 3,247 r.

Several animals died suddenly during or shortly after irradiation; postmortem examination revealed fresh and extensive hemorrhage from the tumor tissue.—*Arthur A. Brewer, M.D.*

Chalecke, William E., Jones, Glenn E., Miller, Leon L., Steinhausen, Theodore B., and Strain, William H. Iodinated organic compounds as contrast media for radiographic diagnoses. vi. *Radiology*, August, 1947, *49*, 131–136.

The authors report the results of experimental use of a 50 per cent emulsion of pantopaque (ethyl iodophenylundecylate) for retrograde pyelography and cystography, hysterosalpingography and intravenous injections, and a 70 per cent emulsion for bronchography in dogs. Both emulsions are readily injected through needles and catheters of small bore. The emulsions are prepared with the aid of a surface active agent (oleyl methyl taurine) and have the property of coating and adhering to mucosal surfaces.

The illustrations of the bronchograms of dogs are striking and show excellent detail of the bronchial branches. Films were made at intervals of five to ten minutes after instillation. Distribution is good and apparently little affected by this time interval. Emulsion is seen in the smaller radicles on the day following the original study. No definite toxic reactions have been observed. The illustrations of retrograde pyelographic studies are also excellent. Delineation of the calyces was present for some time after the medium had run out, in some instances several days. It is uncertain whether these emulsions are suitable for intravenous work.—*Chauncey N. Borman, M.D.*

George, Murray P., Mahoney, Earle B., Pearse, Herman E., and Strain, William H. Iodinated organic compounds as contrast media for radiographic diagnoses. vii. *Radiology*, August, 1947, *49*, 137–142.

The authors report clinical tests of the use of 50 per cent emulsion of iodophenylundecylate for visualization of light empyema cavities. This emulsion has the property of coating and adhering to the walls of a cavity, producing a more perfect delineation than is obtained with other solutions. The medium is distributed to all parts of the cavity by respiratory movements, posturing is not necessary and it is easily and completely removed by saline lavage. If a coagulum of pus is present the medium tends to collect on the surface of the coagulum. Relatively small amounts of the medium are required with a minimum of discomfort to the patients and no toxic reactions have been observed.—*Chauncey N. Borman, M.D.*

Jones, Glenn E., Chalecke, William E., Dec, Joseph, Schilling, John A., Ramsey, George H., Robertson, Harold D., and Strain, William H. Iodinated organic compounds as contrast media for radiographic diagnosis. viii. *Radiology*, August, 1947, *49*, 143–151.

Suspensions of tetraiodophthalimidoethanol were administered to dogs with experimentally produced marginal ulcers and more complete and more accurate delineation of the lesions was noted when compared to the appearance with barium sulphate suspensions. Additional advantages which are claimed for the new contrast medium are greater palatability, no increase in toxicity and less tendency to settle. Double contrast enemas in dogs were also more satisfactory with the iodinated medium than with barium sulphate.—*J. N. Ané, M.D.*

Halberstaedter, L., and Ickowicz, M. The early effects of x-rays on the ovaries of the rat. *Radiology*, April, 1947, *48*, 369–373.

As regards alterations in the ovary in the first few hours following irradiation, a diversity of opinion exists.

Histologic examinations of ovaries of normal and irradiated rats were made to determine whether any difference was present in the distribution of the pyknoses in the follicles.

The histologic studies were performed on ovaries of the following groups of highly inbred albino rats.

A. Control group: 4 rats.
B. Experimental groups: Rats irradiated with 50 to 2,000 r.
 (a) Seven rats, irradiated in the region of the abdomen, the ovaries being exposed directly to the action of the roentgen rays.

(b) Two rats, irradiated in the region of the cephalothorax, the ovaries being protected from direct exposure by means of a lead plate.
(c) Two young rats, irradiated totally.

The radiation was delivered from a Machlett therapy roentgen tube, operated on a multivolt apparatus at 150 kv., 4 ma., 0.5 mm. Al filter, distance 30 cm., 100 r per minute.

The animals were killed four hours after irradiation. Ovaries were fixed in Bouin's fluid and sectioned after embedding in paraffin.

In non-irradiated ovaries pyknoses are largely restricted to follicles whose ovules are in a state of division. When the follicles are examined in entirety, it becomes evident that pyknoses are normally very rare in the granular layer of follicles whose ovule contains a nucleus in a resting state. They are numerous in follicles whose ovule contains a nucleus in a state of division. The evaluation of the effect of roentgen rays on the ovary is best made, therefore, on the basis of findings in follicles which contain an ovule with a resting nucleus.

Observations have shown that four hours following irradiation numerous pyknoses are evident in the granular layer of the large follicles irrespective of whether the nucleus of the ovule is in a state of division or rest. Pyknoses were found, moreover, in follicular cells of young follicles in rats which had been irradiated, but never in corresponding follicles of non-irradiated rats. Follicles whose ovule is in a state of division show pyknoses in cells of the granular layer more frequently after irradiation than normally. A sufficient dose of roentgen rays produces lesion of the ovaries of a rat as early as four hours after irradiation.

The results were best defined with doses of 2,000 r delivered in the abdominal region. A pronounced pyknotic lesion was also observed in the rat which received 400 r in the abdominal region. The reaction of the ovary is not the same when it is not directly exposed to the roentgen rays.

No demonstrable difference was found between ovaries irradiated with doses of 50 and 100 r and non-irradiated ovaries. Doses of this magnitude are probably too low to evoke pyknotic lesions in the ovary within an interval of four hours.

Four hours after irradiation with a sufficient dose of roentgen rays pyknoses are in evidence in follicles whose ovule contains a resting nucleus, as well as in primary follicles.—*Stephen N. Tager, M.D.*

Hamilton, J. G. The metabolism of the fission products and the heaviest elements. *Radiology*, September, 1947, *49*, 325–343.

An investigation of the assimilation, distribution, retention, and excretion of fission products and the heaviest elements in the rat has been conducted at the Crocker Radiation Laboratory of the University of California. In order to protect the personnel working in the field of atomic energy information was needed concerning the behavior of these radio-elements following their introduction into the body by the three major portals of entry, namely inhalation, oral ingestion, and through cuts and abrasions of the intact skin. The fission of uranium results in the production of thirty-four radioactive elements and there have been identified nearly two hundred radioactive isotopes of this large number of elements that arise from fission. Only one fission product, radioiodine, had been studied sufficiently to permit an evaluation of the amount that could be tolerated within the body without producing damage. A table is presented showing the metabolism of the principal members of the long-lived fission products and certain of the heaviest elements in man and the rat following parenteral and oral administration. Only five of the listed fission products are absorbed from the digestive tract to a significant degree (strontium, barium, tellurium, iodine, and cesium). Strontium and barium are deposited and retained to a high degree by the skeleton. Iodine is accumulated and retained by the thyroid. Tellurium shows some accumulation in the kidneys and blood with a rather rapid rate of release from these tissues. Cesium is distributed quite uniformly throughout all of the tissues, the greatest accumulation occurring in the muscle, and it is quite promptly excreted. The distribution of these five fission products following oral absorption is indistinguishable from their metabolism after parenteral administration and they were also found to be readily absorbed through the lung.

Many of the long-life fission products and the actinide elements are promptly deposited and show long retention in the skeleton. Radioautographs show that, with the exception of strontium, they are not deposited in the mineral structure of bone but rather appear to be localized in and adjacent to the osteoid matrix. Of

the fission products and actinide elements that are deposited in bone, all except possibly columbium are released at a very slow rate. This places them in the category of radium so far as retention in the skeleton is concerned. Some of them, particularly most fission products, have half-lives very much shorter than radium and they emit beta particles instead of alpha particles and this somewhat reduces their hazardous nature. Of the fission products and actinide elements which emit alpha products and which accumulate in the osteoid matrix, their disintegration will result in bombardment of the radiosensitive bone marrow.—*Robert K. Arbuckle, M.D.*

Chamorro, A. Bases biologiques d'une action associée des hormones et des rayons X sur la cellule cancérisée de certaines glandes, sous controle hormonal. (The biological bases of an associated action of hormones and roentgen rays on the cancerous cells of certain glands under hormonal control.) *Compt. rend. Soc. de biol.* January, 1948, *142*, 3–4.

Development of resistance to irradiation of a small fraction of cancerous cells is the explanation of the recurrence and ultimate metastasis of malignancies, especially in protracted types of therapy. To overcome this, a combination of hormonal and roentgen treatment seems to be rational for malignancies of glands directly or indirectly influenced by hormones. The point is to increase the radiosensitivity of these resistant cells by stimulating them to premitosis through hormonal therapy.

The dose of the hormone and the roentgen radiation administered depends on the type of the glandular malignancy. For example, in the case of the epithelioma of the mammary gland, give estrogen (natural or synthetic) 3 to 5 mg. per day plus 5 mg. of progesterone daily, for ten days. On the eighth day begin roentgen therapy and in six days give 900 to 1,200 r per field. Repeat this associated treatment four or five times. A rest of one to two weeks between each series of treatment is necessary.

The epitheliomas which can be thus benefited are those of the:

(1) Mammary glands (estrogen and progesterone);
(2) Prostate (propionate of testosterone 25 mg. daily for 14 days);
(3) Thyroid (thyrotropic hormone 200 U. C. per day for 14 days or propylthiouracil 25 to 50 mg. per day for 12 days);
(4) Ovary (gonadotropic hormones);
(5) Uterus (estrogen plus progesterone);
(6) Submaxillary glands (androgen);
(7) Hypophysis (estrogen).—*J. N. Sarian, M.D.*

Landauer, Robert S. Application of the inverse-square law to oil-immersed tubes. *Radiology*, February, 1947, *48*, 175–177.

According to the inverse-square law, radiation intensity at a given point varies inversely as the square of the distance from the source. Two prerequisites are included but often overlooked: (1) that radiation be emitted from a point source, (2) that no absorbing or scattering media intervene between the source and the site in question.

In view of the doubt expressed regarding the validity of this law as applied to small oil-immersed tubes (140 kv., peak, or less) radiation intensity determinations were made at various levels, between 5 and 20 inches, using a Victoreen r-meter and a specially built wooden structure. Eleven different tubes were tested. The averages obtained indicate that the inverse-square law may be applied in calculating intensities at distances between 5 and 20 inches with an average error of not over 1 per cent, and a maximum error of ± 6 per cent.—*William H. Shehadi, M.D.*

Trout, E. D., and Atlee, Z. J. Low-absorption roentgen-ray measurements from 500 to 1,000 kilovolts. *Radiology*, June, 1947, *48*, 604–609.

An extension of earlier studies is presented on low-absorption roentgen-ray measurements using a beryllium window, permanently evacuated tube, at voltages up to 1,000 kv.

A multisection million volt tube with beryllium window of $1\frac{1}{4}$ inches diameter and inherent filtration of 3 mm. of beryllium (equivalent to about 0.05 mm. of lead) was used. All measurements were made with a Victoreen thimble chamber at 100 cm. distance, 500 to 1,000 kv., and 0.1 ma. to 3.0 ma. Because of filament space-charge limitations, a maximum of 500 kv. at 1.0 ma. was used. Absorption data were taken for copper and lead.

Results are given in the form of graphs showing absorption curves for copper and lead, half-value layers in lead and a graph for determining the inherent filtration from the half-value layer in lead for voltages of 500 to 1,000 kv. The half-value layer at 1,000 kv. with no added filtration was 1.1 mm. of lead as against

1.9 mm. for the conventional million volt tube.

Examples of output obtainable from this tube were as follows: (1) at 1,000 kv. and 3 ma. (the full load rating), at 50 cm. distance, 264 r per minute, (2) at 2 cm. distance, in contact with the beryllium window, 165,000 r per minute.

A graph for determining inherent filtration from the half-value layer in lead of any roentgen tube operating in the range of 500 to 1,000 kv. is presented.

The authors are of the opinion that beryllium windows are indicated for tubes operating up to 750 kv. but that at and above 1,000 kv., emphasis should be placed on the window thinness rather than its composition.—*E. D. Hudack, M.D.*

ROGERS, T. H. High-intensity radiation from beryllium-window x-ray tubes. *Radiology*, June, 1947, *48*, 594–603.

Beryllium has the lowest absorption coefficient of any material likely to be used for windows in roentgen tubes. Originally beryllium was used in the internal hoods of roentgen tubes to stop secondary electrons while allowing the transmission of roentgen rays.

The first commercially produced tubes with vacuum-tight beryllium windows were designed primarily for roentgen-ray diffraction where the use of long wavelengths necessitated reduction of window absorption to a minimum. The low-absorption window with its advantages soon lent itself to use in microphotography and industrial work. As these tubes became used more widely, a demand arose for beryllium window roentgen tubes with larger windows. Aside from permitting a greater afflux, beryllium can be located very close to the focal spot. This is not feasible with other low-absorption materials. An intensity of 2,330,000 r per minute is obtainable at 2 cm. (target face to outer surface of window) at 50 kv. and 20 ma.

These high outputs lend themselves to new exploits such as: (1) sterilization of vaccines while the antibodies remain unaffected, (2) sterilization of suture material without heating, (3) sterilization of foods without subjecting them to flavor destroying temperatures. In therapeutic radiology while the high intensity in itself is not directly an advantage, it does afford a wide range of dosage rates in its application to intracavitary, "grenz" ray and "skin therapy." The possible role this achievement may play in atomic research and industry is alluded to. Several specific photochemical reactions are mentioned, in which the color changes in precious stones and the fluorescence in other substances can be used for qualitative and quantitative analysis in research.

Suitability of various instruments for measuring the r per minute output of the radiation is discussed and references to the literature discoursing on these instruments are cited.

A tube of new design, constructed on an experimental basis making all the radiation available in the continuous processing of materials is discussed. This tube has a domed window which makes possible a 180 degree radiation field. It is operable with a load of 60 kv. at 100 ma. with a predicted output of approximately 5,000,000 r per minute available over 25 sq. cm. —*E. D. Hudack, M.D.*

MALLET, LUCIEN, and MAURIN, ROBERT. A study of quality and origin of parasitic radiation from the target of an x-ray tube. *Radiology*, June, 1947, *48*, 628–632.

The studies were made on a machine of the United States Army Field Unit type. It was found that roentgen rays were produced not only at the principal focal point but also on the remainder of the tungsten target and the copper stem. The intensity and quality of the radiation from these zones were studied by three methods: (1) independent micro-ionization chambers, (2) the Strauss dosimeter, (3) blackening of a film. It was found that radiation from the principal focal point was of the greatest wavelength, whereas rays from the periphery of the target and the supporting stem were more penetrating. The radiation was most penetrating at the point of exit from the tube when a limiting diaphram with a large aperture was used.

The details of the experiments are clearly described and the explanations of the phenomena are graphically illustrated. These findings are of significance for both roentgenography and radiotherapy.—*Oliver P. Winslow, Jr., M.D.*

LANGE, KURT, and EVANS, ROBLEY D. Absorption of radon through the skin and its exhalation through the lungs. *Radiology*, May, 1947, *48*, 514–516.

The authors describe their method of measuring the absorption of radon through the skin and its exhalation through the lungs in 3 patients under treatment with radon ointment. Their method is convenient and yet practical,

and they found that appreciable amounts of radon gas applied in ointments were absorbed through the intact skin and through opened wounds and affected deeper structures by absorption into the blood stream and thence transportation by the blood stream to the deeper tissues. They thus state that the efficiency of radon ointment in the supplying radon and its alpha irradiation to underlying tissues is quite high.—*Moris Horwitz, M.D.*

Jacobson, Leon O., and Marks, E. K. The hematological effects of ionizing radiations in the tolerance range. *Radiology*, September, 1947, *49*, 286–298.

Knowledge of the biological effects of radiations in general and of certain radiations and radioactive materials specifically was so superficial prior to World War II that the medical and biological divisions of the Plutonium Project were organized. The objectives were essentially to study the fundamental and comparative action of radiations and radioactive materials and to apply these findings to the protection of personnel or individuals potentially in danger of exposure to these physical hazards. Data were required on the biological effect of chronic irradiation in the region of the "tolerance dose." Externally originating radiation, "whole body," had to do with gamma rays, roentgen rays, beta rays, and neutrons. This study presents data on the findings in the peripheral blood of animals exposed to roentgen rays and gamma rays. Rabbits, mice, and guinea pigs were used. Blood studies included erythrocytes, hemoglobin, leukocytes, the differential leukocyte count, platelets, reticulocytes, and in special instances erythrocyte diameter. After control preirradiation exposure counts were made at least twice, the animals were placed in cages in fixed positions to receive definite exposures of deliberately planned irradiation from a large centrally placed radium source. The species and substrains of laboratory animals were divided into groups and exposed to doses of 0.1, 1.1, 2.2, 4.4, and 8.8 r, some for eight hours per day and others for twenty-four hours per day, six days weekly. The animals were observed while thus exposed over periods now well extended beyond three years.

Significant Findings

1. In female mice, biological effects appear in the absence of detectable hematological change. Ovarian tumors developed in mice exposed to 0.1 and 1.1 r per day while no detectable changes in peripheral blood occurred at any time during the three years' exposure to these doses.

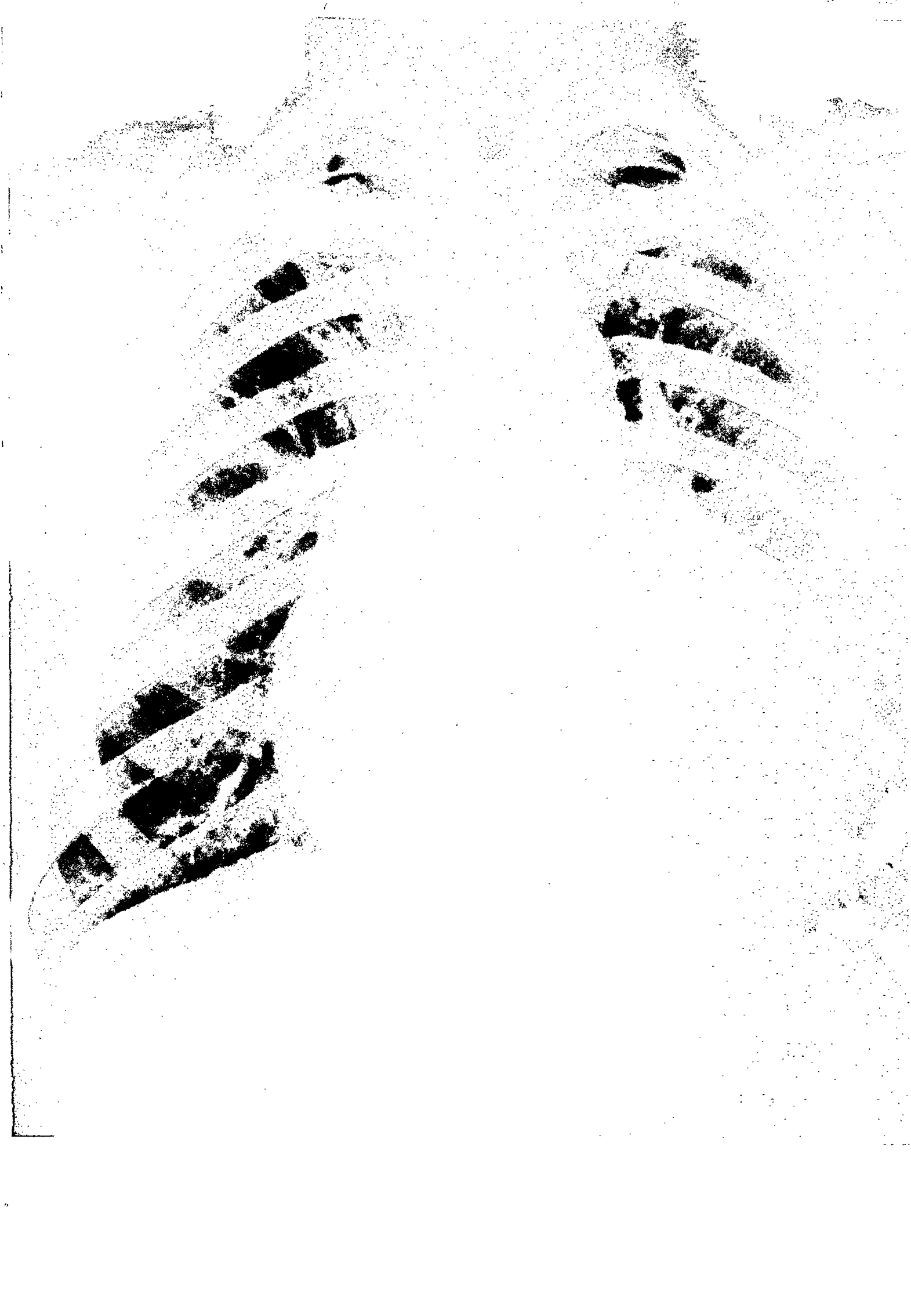
2. Findings commonly believed to indicate chronic irradiation damage (lymphocytosis, eosinophilia, monocytosis) did not occur in any of the three species exposed clinically to doses between 0.1 and 8.8 r per eight hour or twenty-four hour day.

3. Lymphocyte reduction was the earliest abnormality noted in the peripheral blood of these three species after chronic exposure.

4. There was no histologic evidence of abnormality of the blood-forming tissues in the animals which developed a lymphopenia.

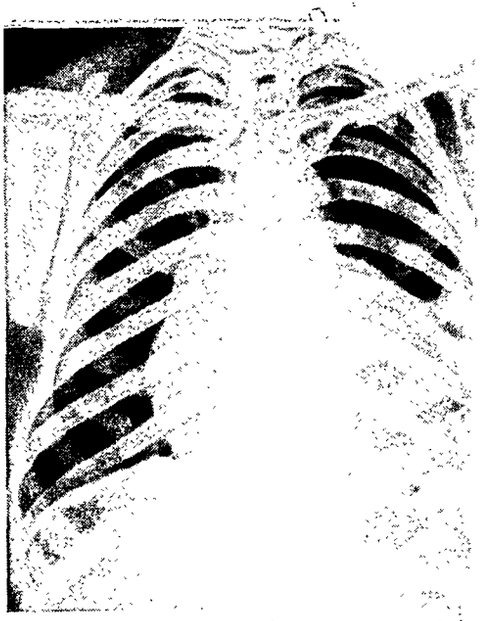
5. Severe anemia (acute onset) was common cause of death of guinea pigs exposed in the 8.8 and 4.4 r exposure level.

The personnel of the Plutonium Project were divided into (1) control group and (2) work hazard group depending on whether or not their work brought them into exposure or potential exposure to physically hazardous materials. Frequent hematological studies were made in these groups (varied from daily to every three months). A leukocyte count of 3,000 per cubic millimeter called for careful special clinical and laboratory studies. Only relatively few instances were encountered in which changes in the peripheral blood of personnel could be attributed to contact with external radiation or the deposition of radioactive materials within the body, and no changes occurred which were referable to radiation exposure in the "tolerance range" of 0.1 r per day as set by the National Bureau of Standards.—*Robert K. Arbuckle, M.D.*



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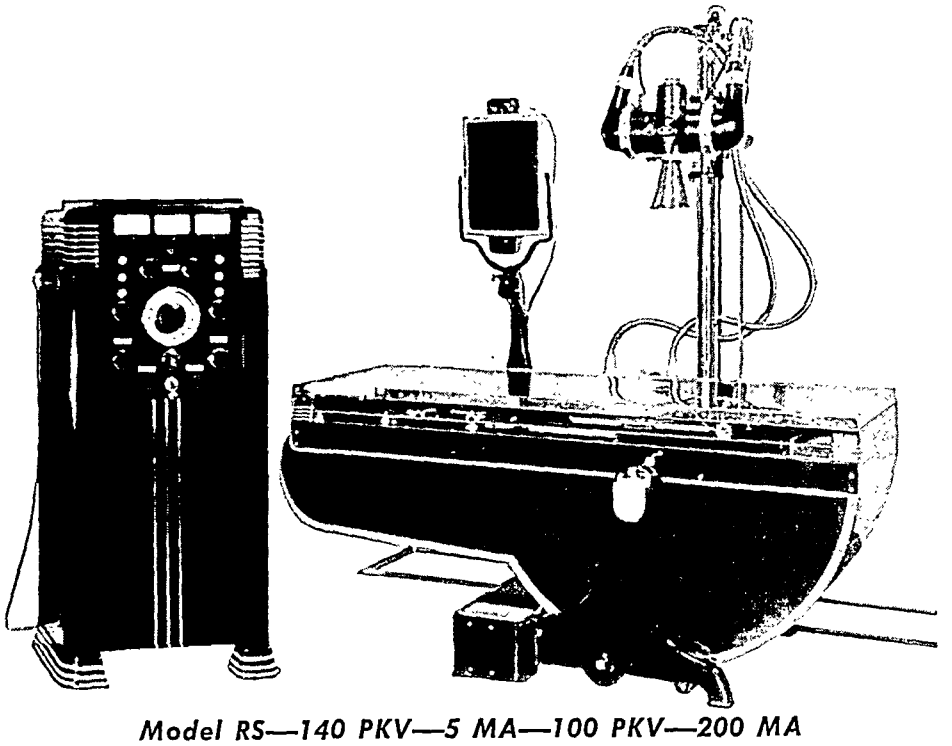
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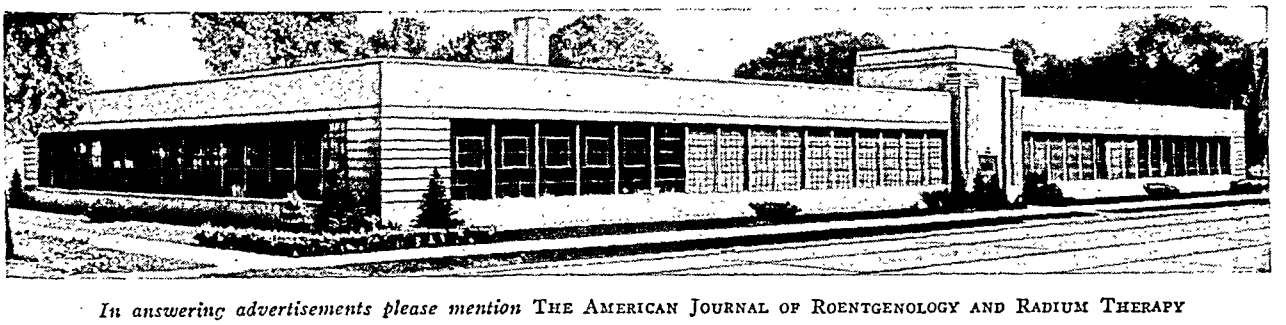
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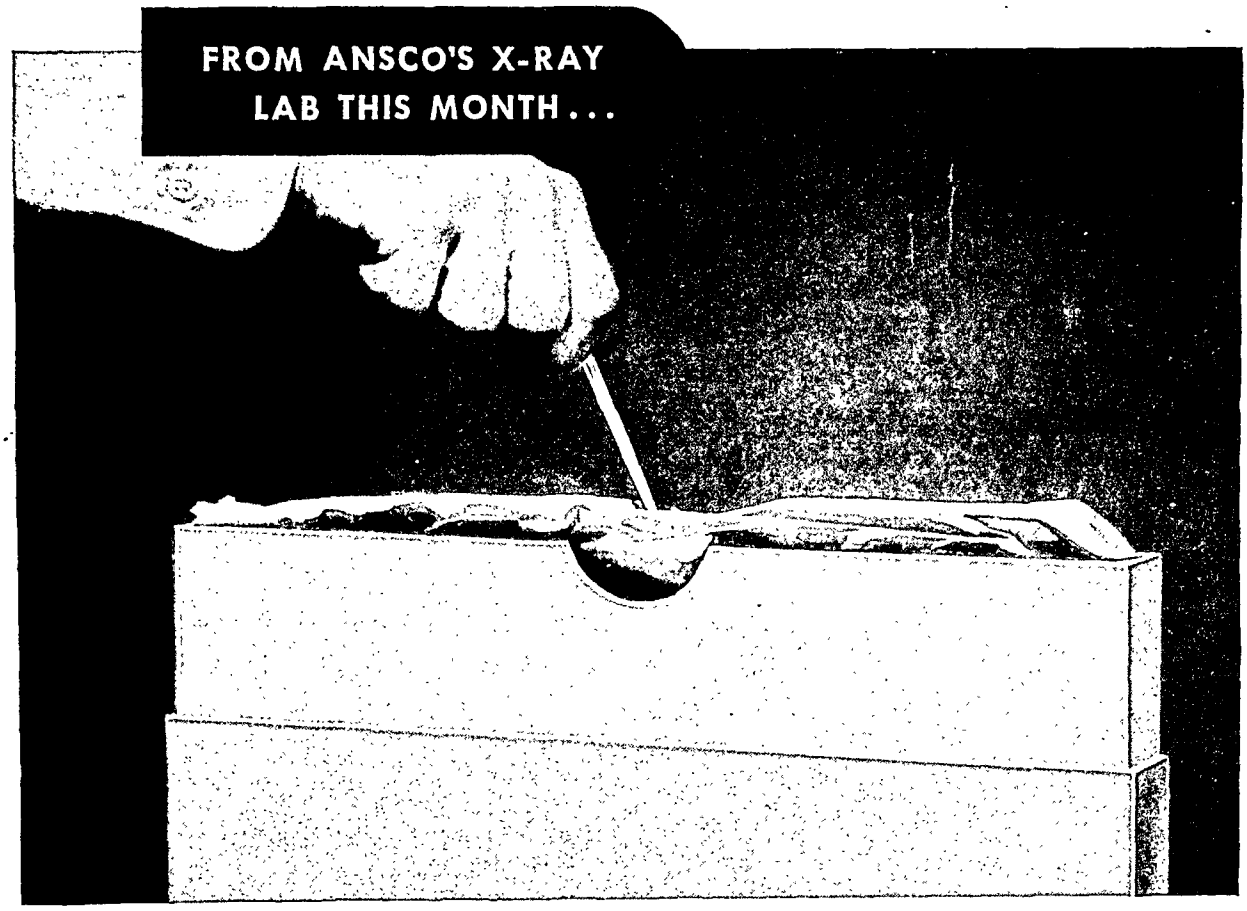
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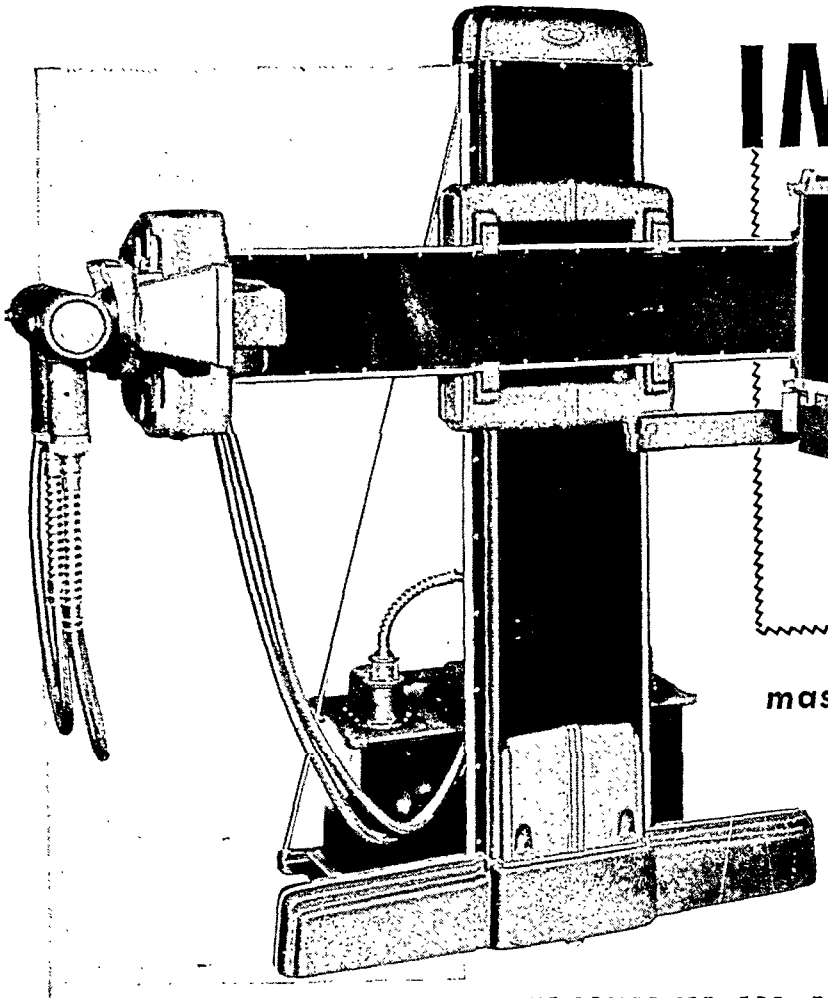
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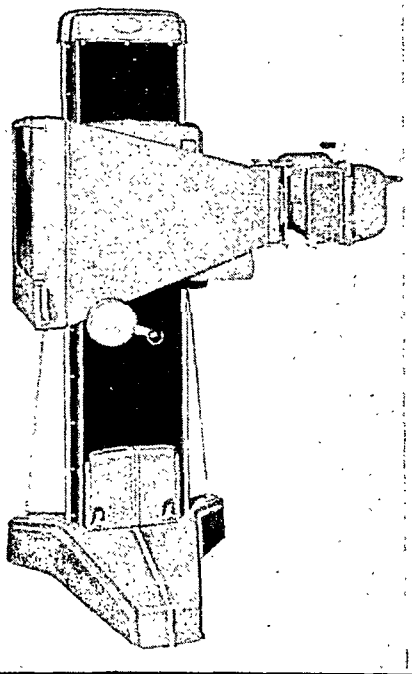
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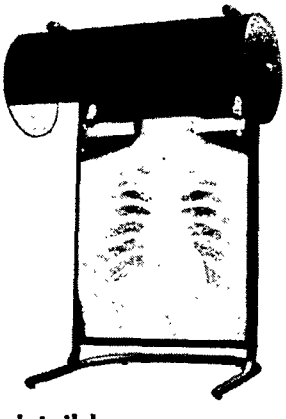
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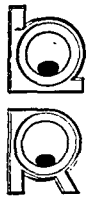
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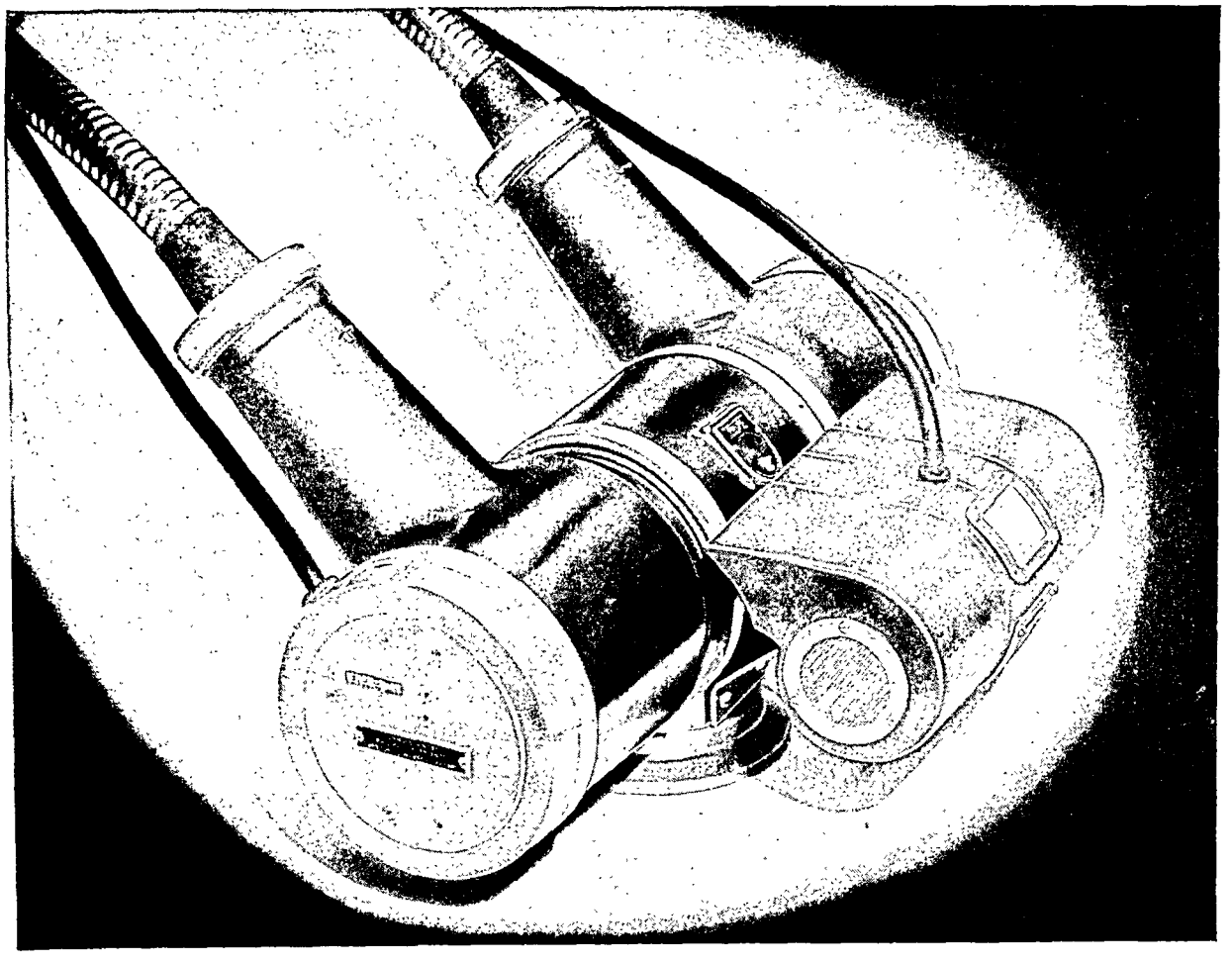
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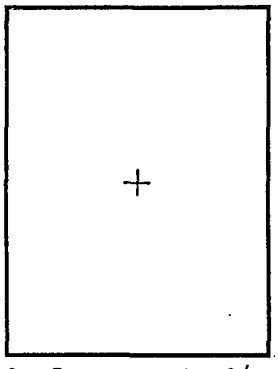
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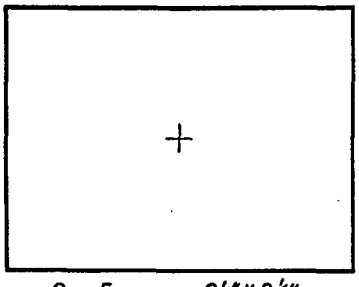
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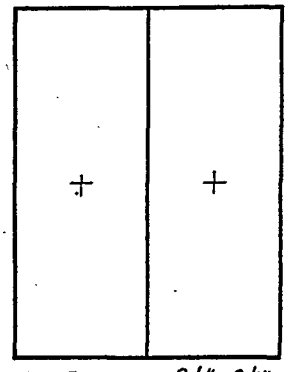
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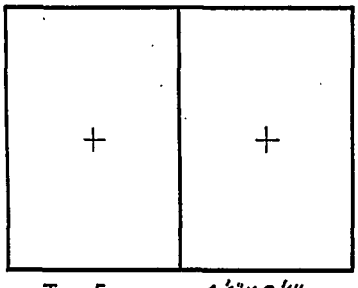
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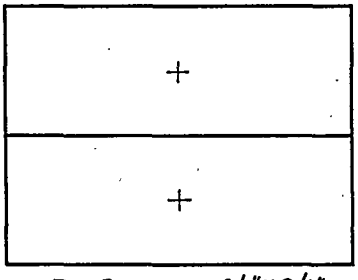
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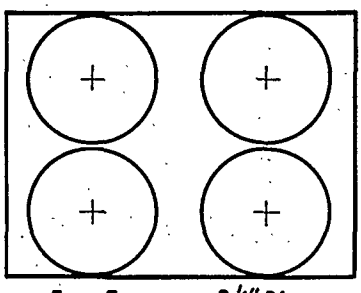
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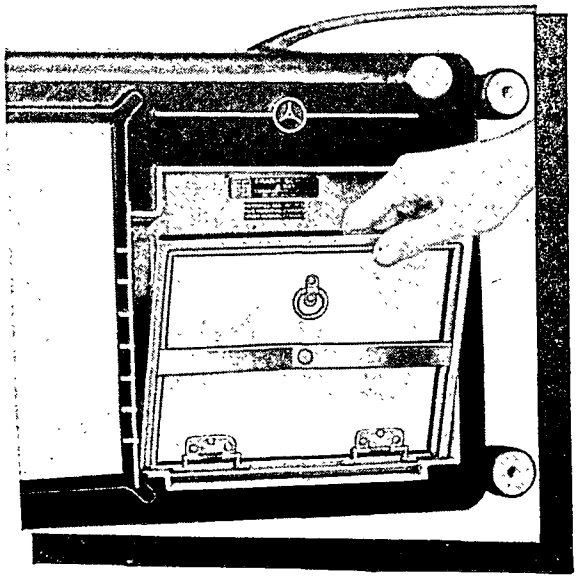
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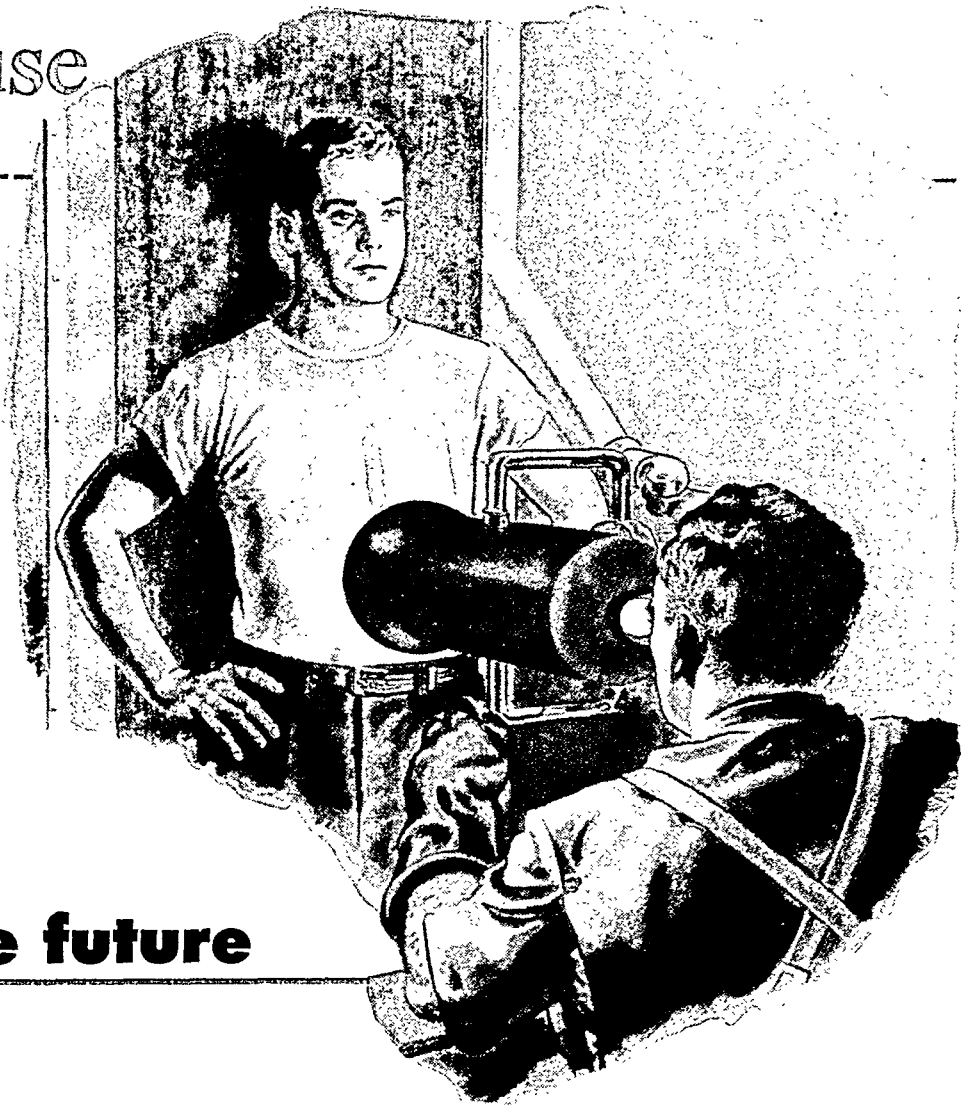
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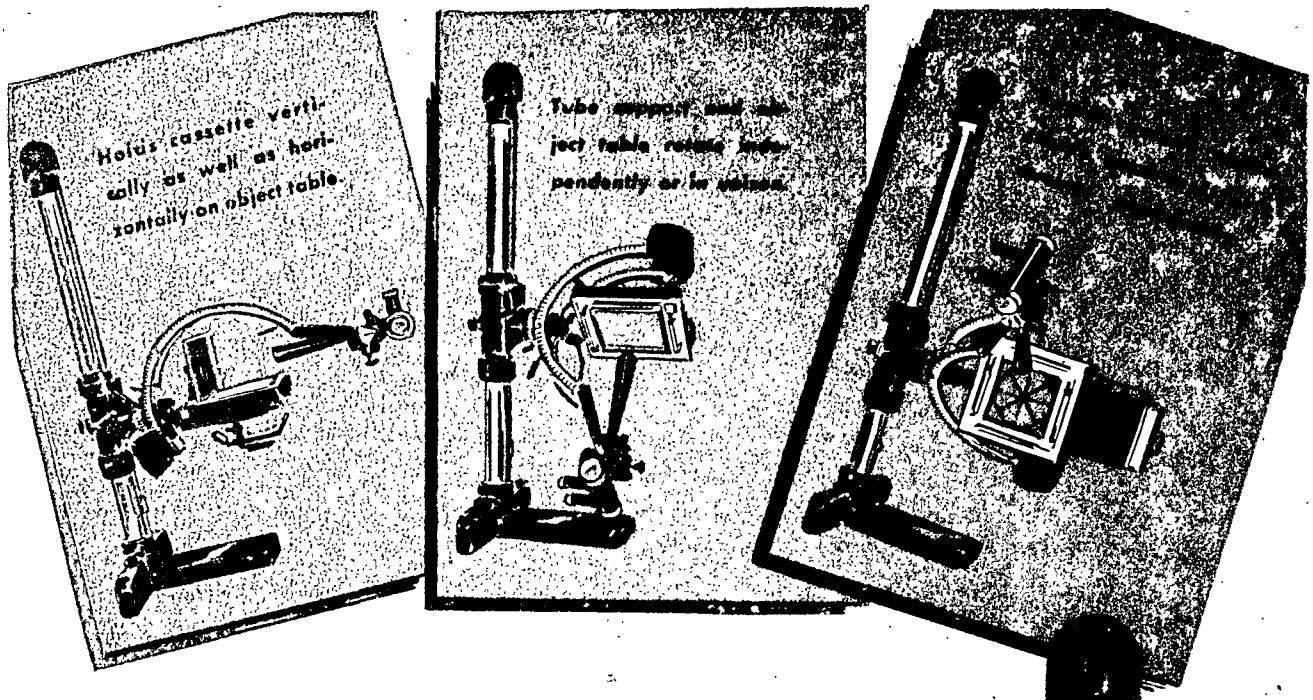
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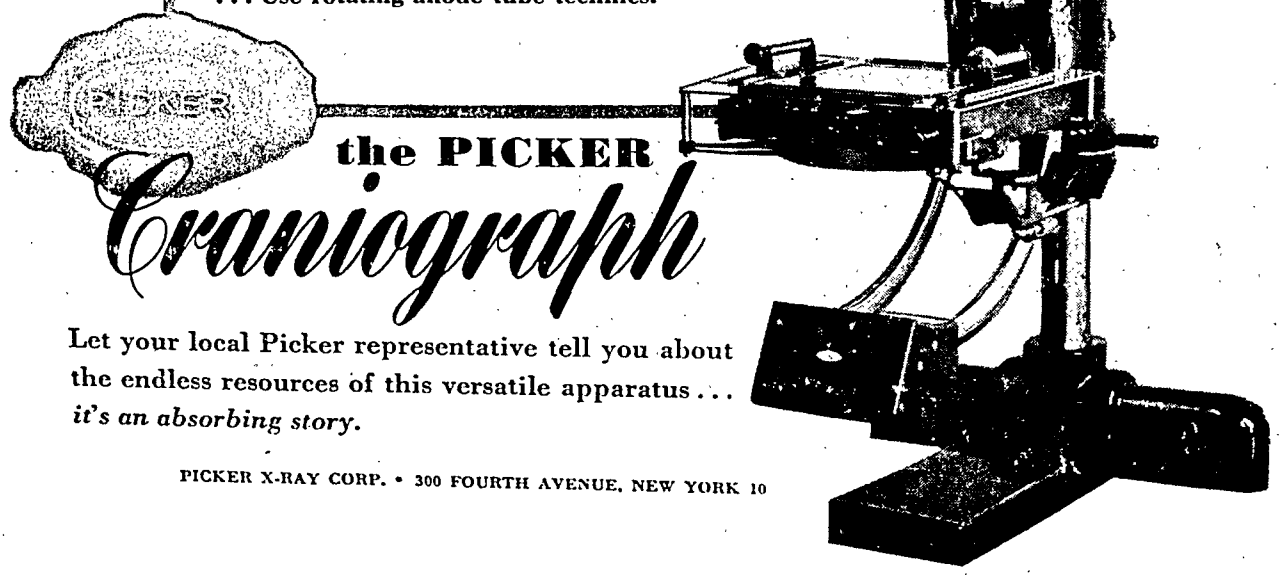
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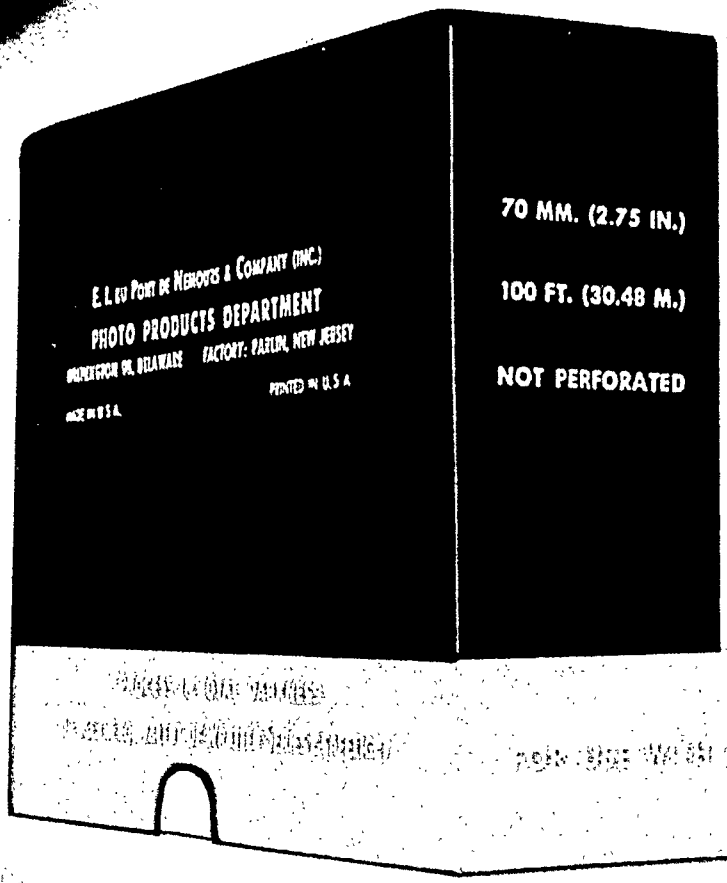
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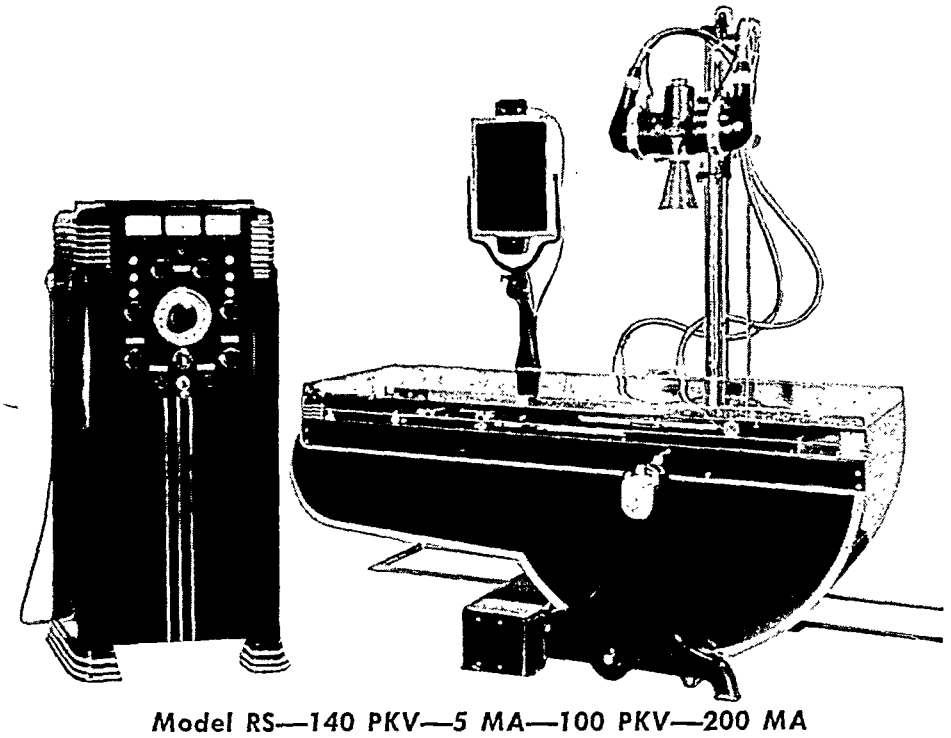
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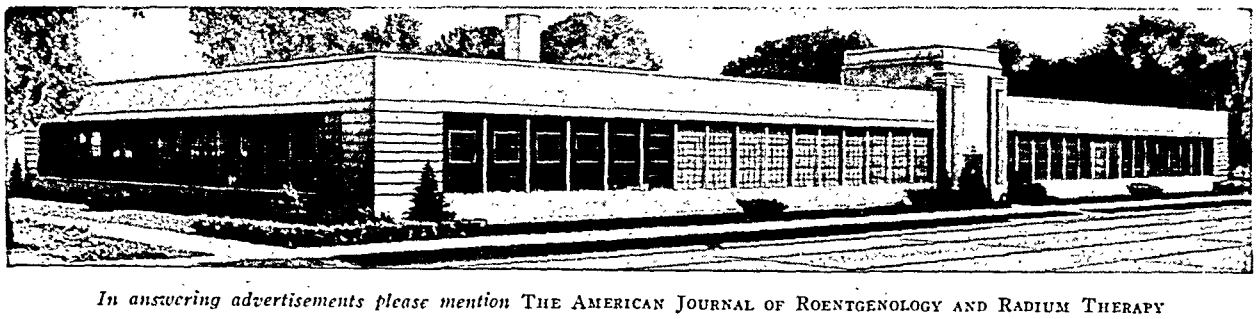
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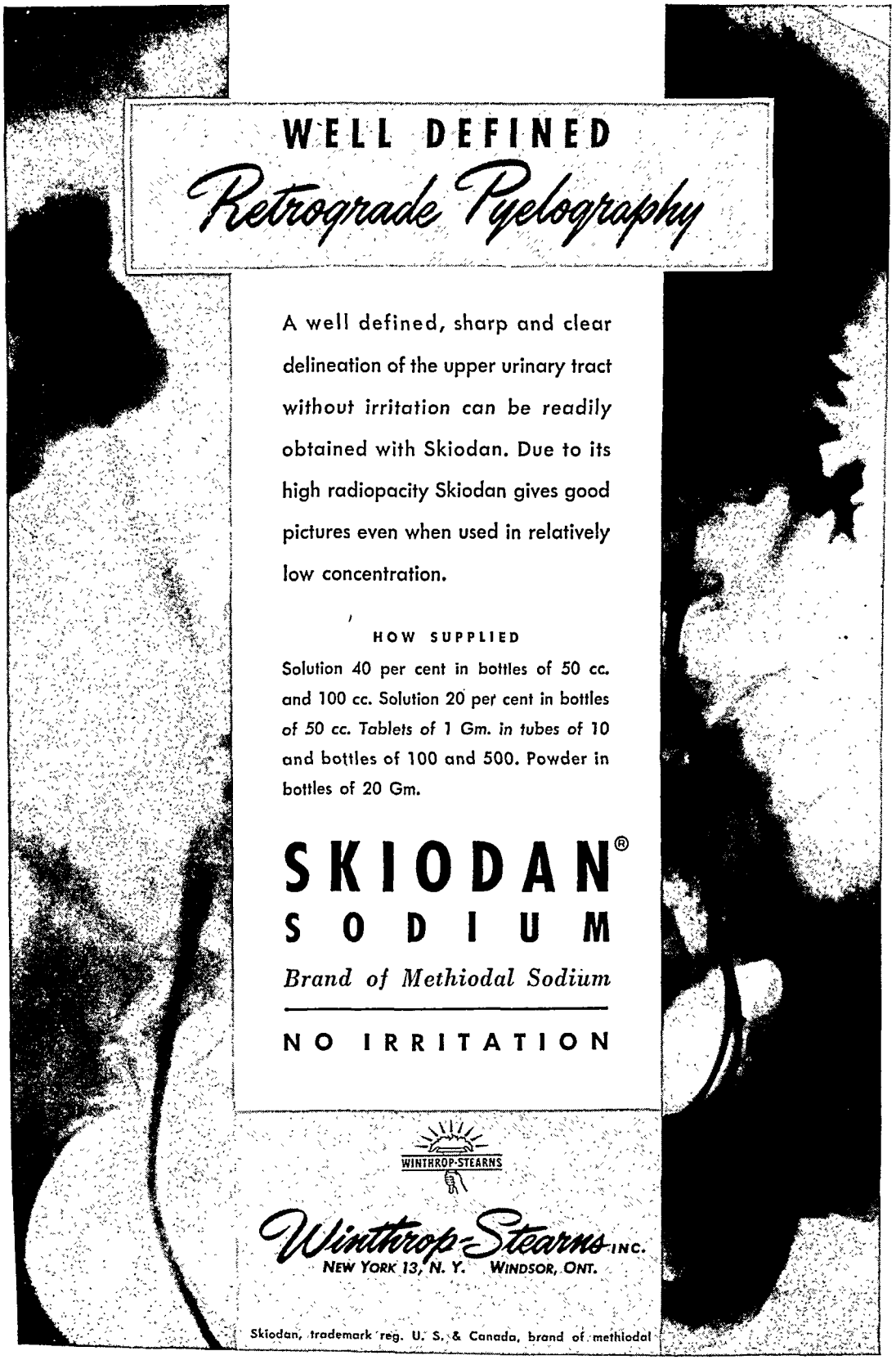


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CONTENTS

The Possibilities and Limitations of Roentgen Diagnosis. Pancoast Lecture LEO G. RIGLER, M.D. 743

The Roentgen Findings in Intracranial Mass Lesions J. GEORGE TEPLICK, M.D., AND PHILIP DORSEY, M.D. 762

Complete Block of the Lumbar Spinal Canal Due to Herniation of the Nucleus Pulposus BERNARD S. EPSTEIN, M.D. 775

The Roentgenologic Diagnosis of Prolapsed Gastric Mucosa CHAPIN HAWLEY, M.D., PAUL D. MEYER, M.D., AND BENJAMIN FELSON, M.D. 784

Arachnodactyly (Marfan's Syndrome) . ROBERT C. MOEHLIG, M.D. 797

The Quantitative Evaluation of Bone Density PAULINE BEERY MACK, WALTER N. BROWN, JR., AND HUGHES DANIEL TRAPP 808

Subacute (Pseudotuberculous, Giant Cell) Thyroiditis and Its Treatment JOHN D. OSMOND, JR., M.D., AND U. V. PORTMANN, M.D. 826

Sarcoma of the Uterus STANLEY B. REICH, M.D. 830

Studies on the Metabolism of Radioisotopes by Various Fungi and Bacteria . I. A. PEARSON, J. M. HAMMER, K. E. CORRIGAN AND H. S. HAYDEN 839

Department of Technique

Portable Projector for Roentgenograms RAYMOND A. DILLON, M.D., AND WILLIAM P. MURPHY, JR., M.D. 847

Editorials

Intussusception WILLIAM A. EVANS, Jr., M.D. 851

Thomas S. Stewart, 1876–1949 . . GEORGE E. PFAHLER, M.D. 853

Percy Joseph Delano, 1899–1949. . . ROBERT F. STOKES, M.D. 854

Society Proceedings, Correspondence and News Items 856

Book Reviews 863

Abstracts of Roentgen and Radium Literature 866

Subject Index to Volume 61 887

Author Index to Volume 61 900

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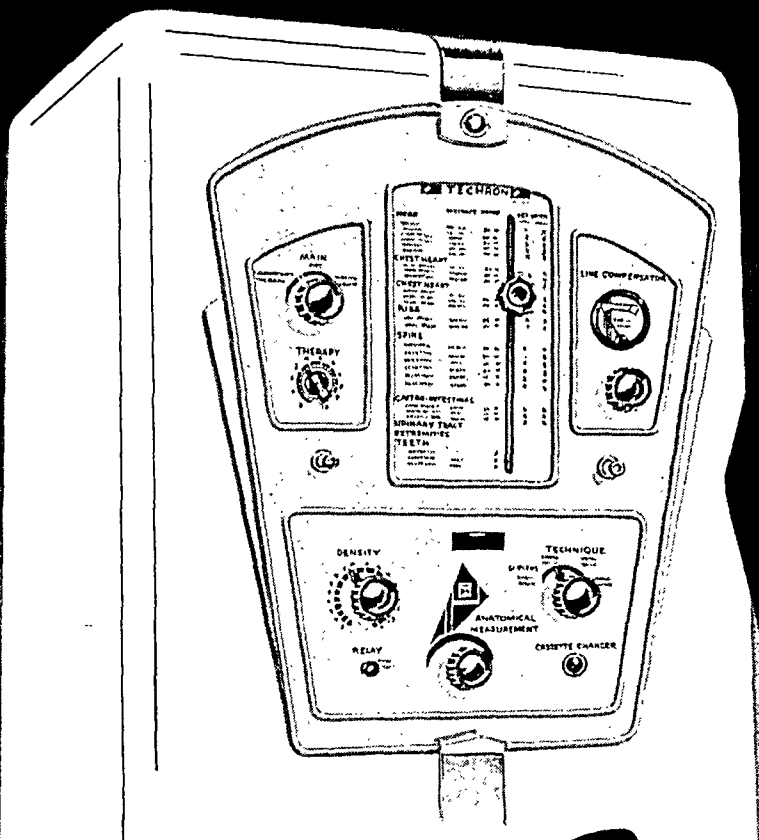
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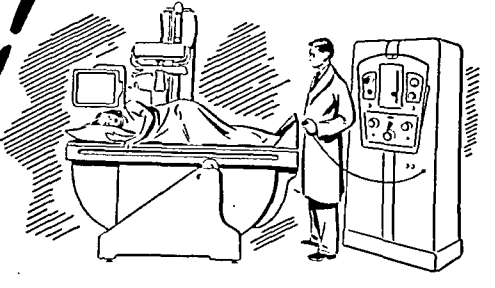
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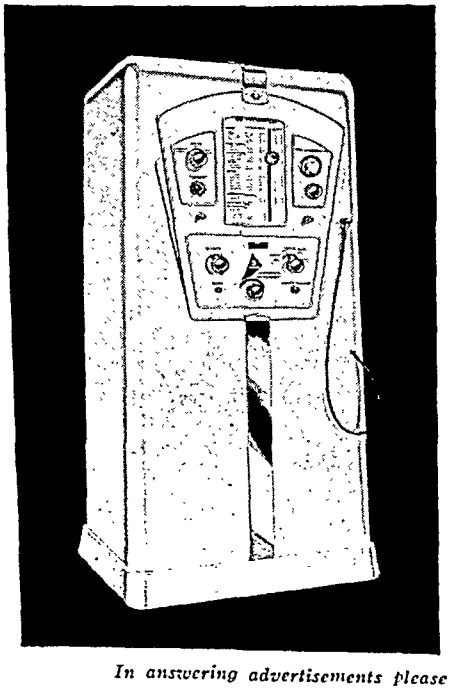
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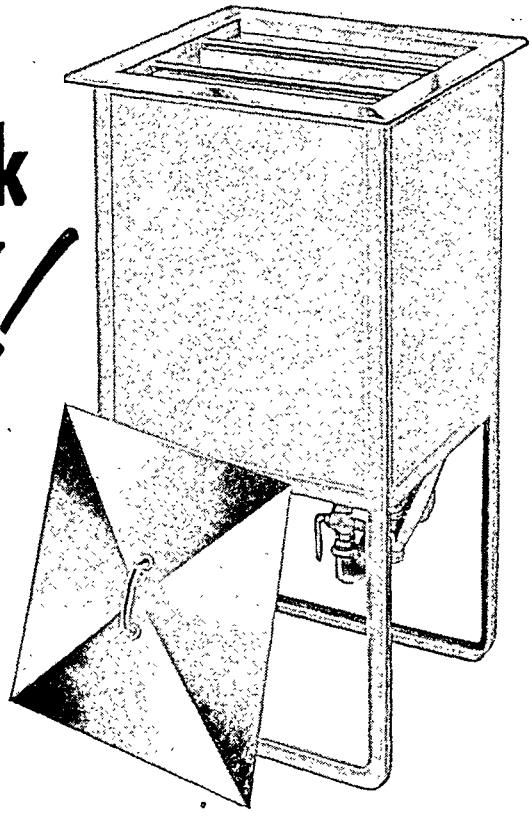
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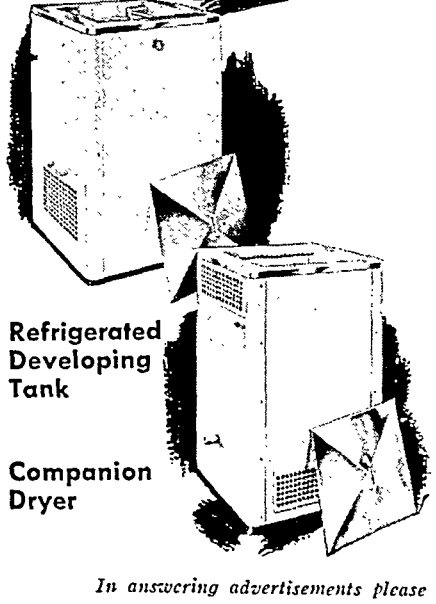


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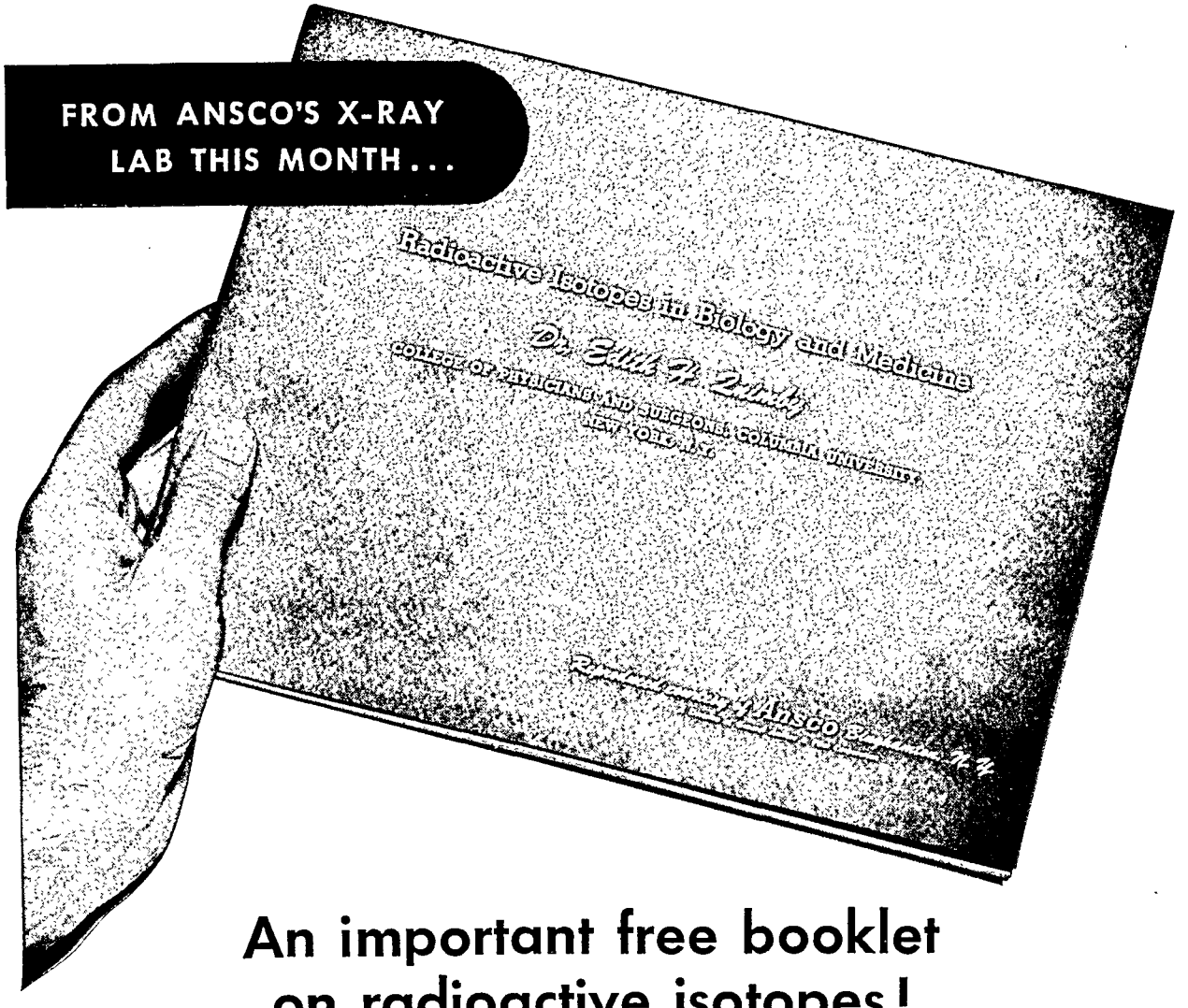
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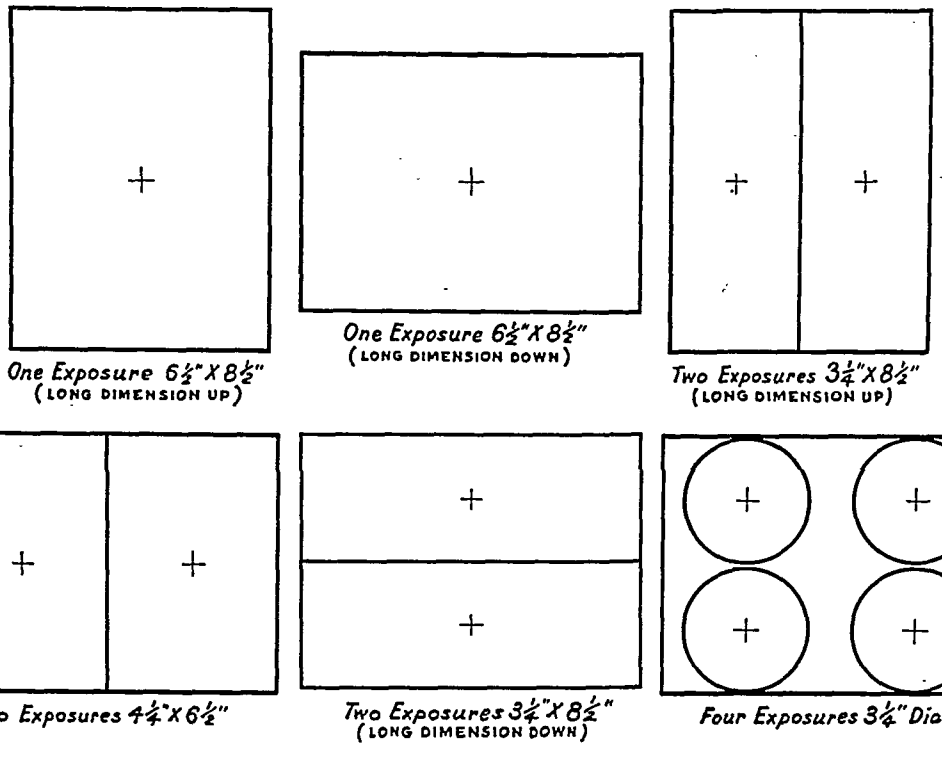
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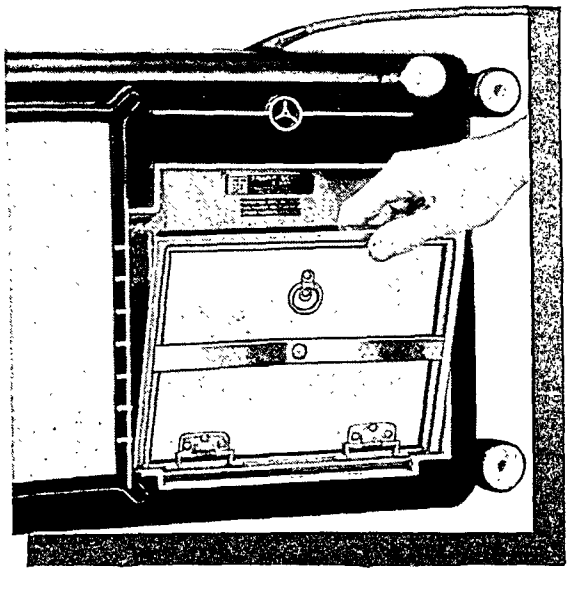
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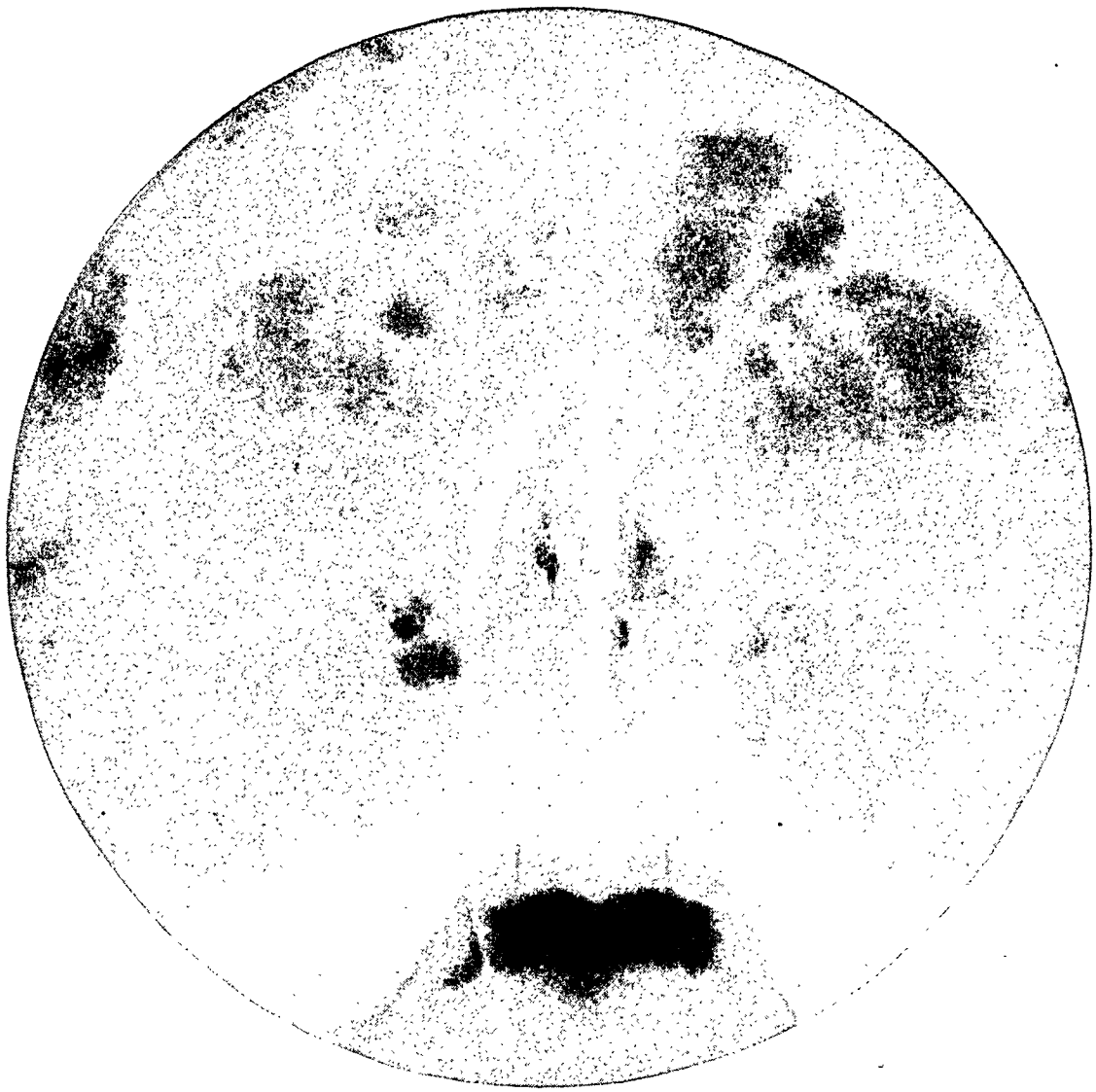


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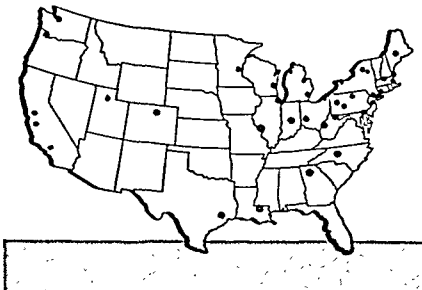
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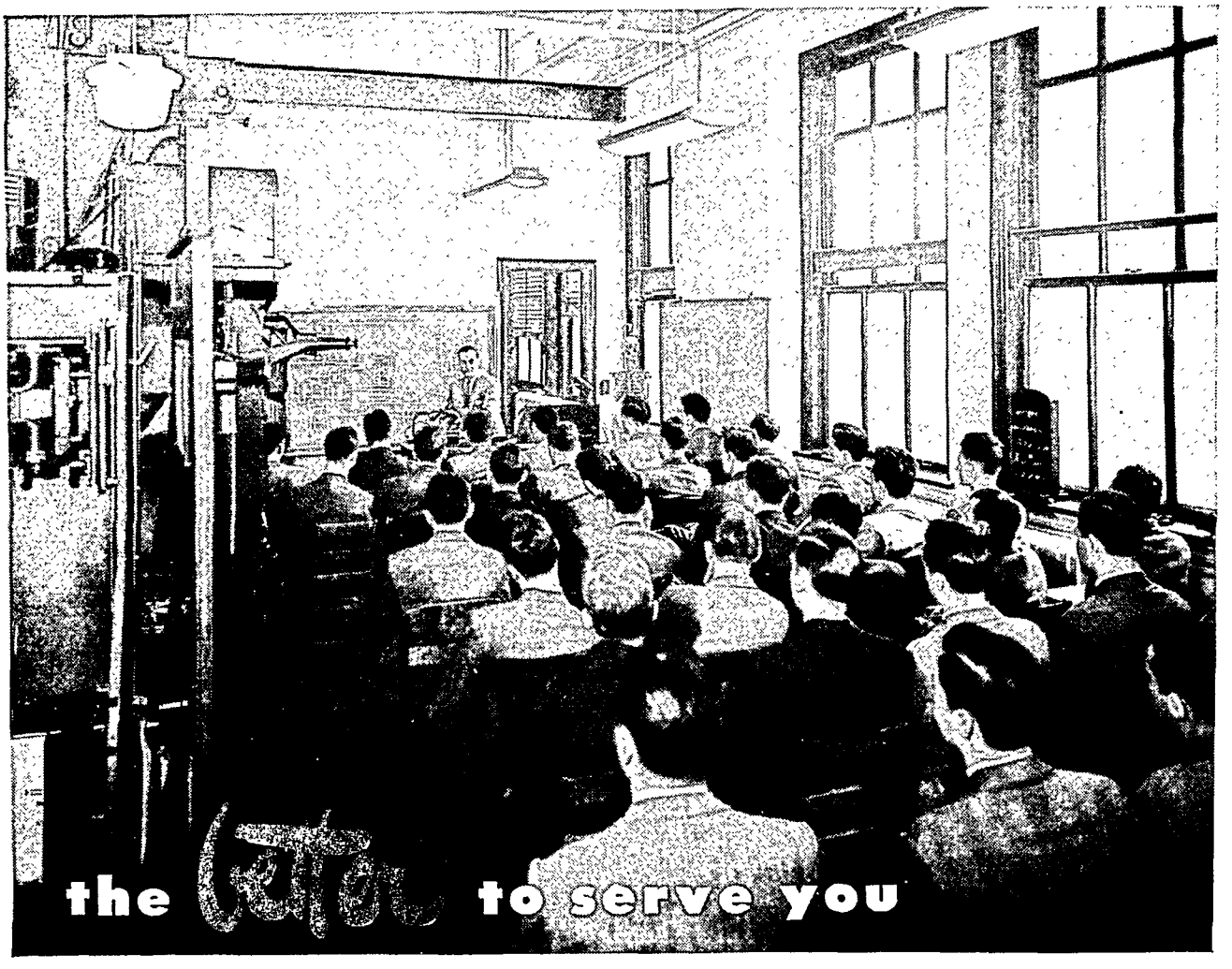
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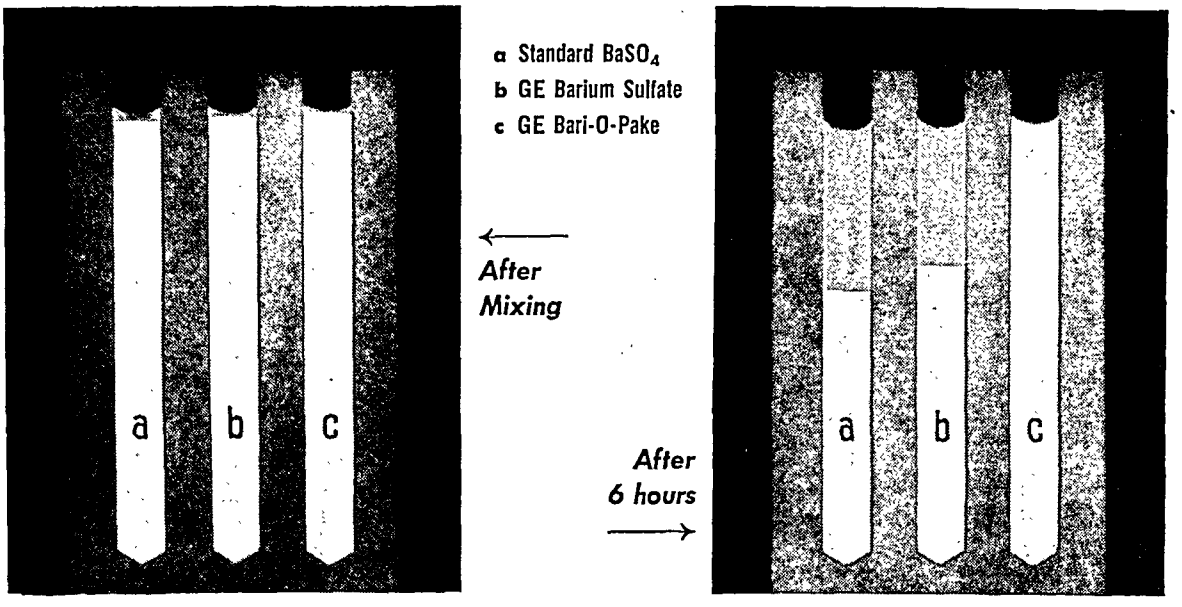


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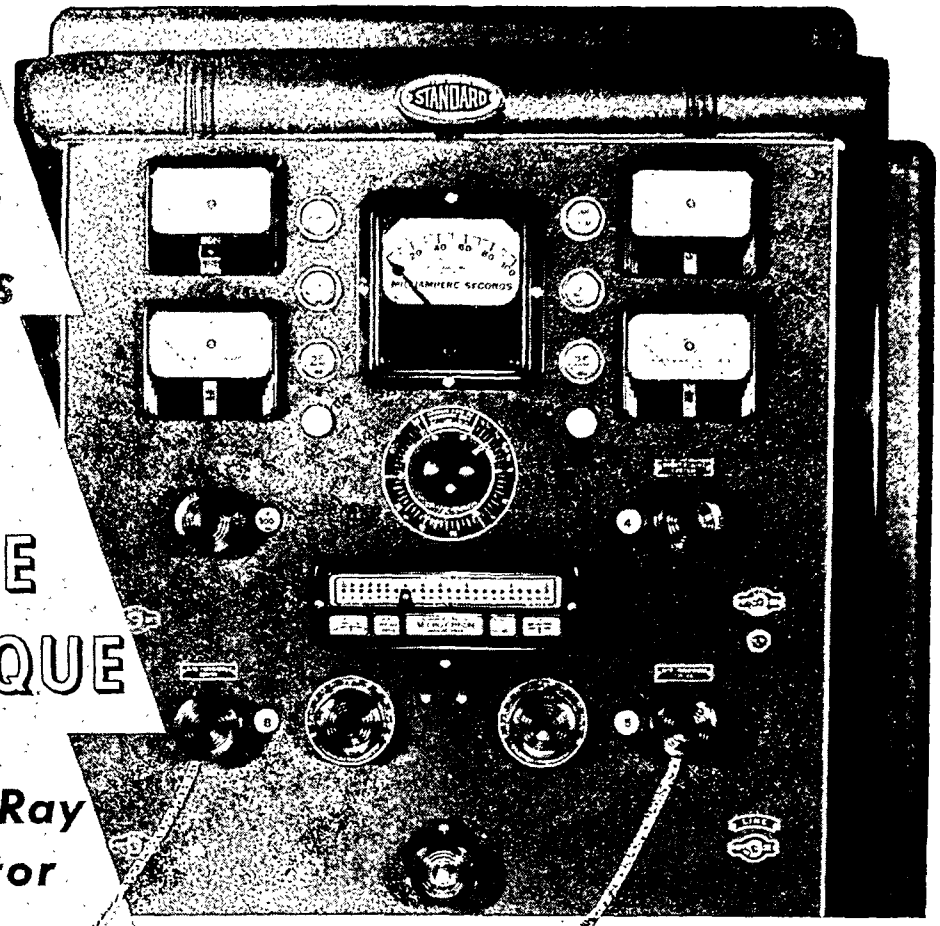
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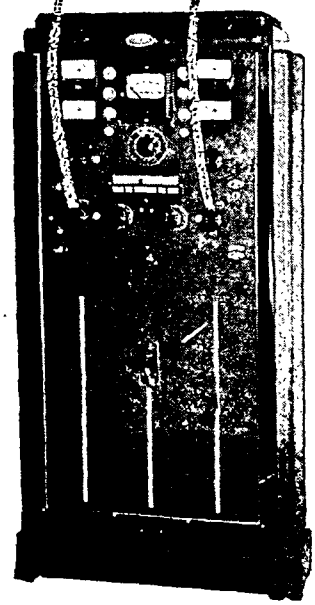
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By LEO G. RIGLER, M.D.

MINNEAPOLIS, MINNESOTA

TO AN American physician, especially a radiologist, who has spent almost his entire life in the Middle West, a visit to Philadelphia is an emotional experience of large dimensions. For not only is this city the very birthplace of our country, but in almost similar fashion Philadelphia gave forth the wellsprings for the development of medicine in America. It is not surprising, therefore, that this community should have a most profound effect upon the development of the youngest of the medical specialties, radiology, during the half century which has passed since its inception. Some two years ago, on the occasion of the semi-centennial of the discovery of the roentgen rays, I undertook the task of reviewing the development of roentgen diagnosis in the United States[28] and I was struck, as any student of medical history would be, with the remarkable contributions of Philadelphia physicists and physicians to the establishment and the progress of radiology. One need only mention the names of Goodspeed, Charles Lester Leonard, Kassabian, Bowen, Snook, Newcomet, Willis Manges and, happily still with us, George Pfahler, to realize what this city has meant to this new science. In that development no one had a greater part than the man whose memory we come together to honor tonight. I am sure that all of you are familiar with the life of Henry K. Pancoast and with his accomplishments. I am sure that the distinguished physicians who preceded me in presenting this lecture have already, far better than could I, detailed some of the debt which radiologists, which physicians, which all people owe to Henry Pancoast for his unremitting devotion to the field of endeavor which he so richly endowed during the years which were permitted him. Perhaps I would do best to quote from the gifted pen of Percy Brown who wrote in this JOURNAL,[6] "For radiologists of the present and the future this life [the life of Henry Pancoast] is a pattern of a kind that all scientific men admire—clean-cut, smooth of edge, true of angle and of dimensional exactitude."

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† The Pancoast Memorial Lecture presented at the Annual Meeting of the Philadelphia Roentgen Ray Society, Philadelphia, Pa., November 6, 1947.

We who did not have the opportunity of working with him obtain from his writings the impression of a man of real intellectual honesty who faced every issue fearlessly and sought only for the truth. Scarcely any man in the history of American radiology has had more honors bestowed on him by his colleagues—certainly few have so well deserved them. A man who is privileged to present a lecture in honor of Henry Pancoast is fortunate indeed.

In a lecture memorializing the work of a great man it seems peculiarly fitting to discuss something which is related to the philosophy of the field in which he worked rather than to present any one specific investigation. Roentgen diagnosis having come of age, it is time to critically examine both the possibilities and limitations of a method which, because of its objectivity, because it appeals to the visual sense, in which we all have the greatest faith, has a certain attractiveness for physicians and for the lay public, inspires a certain confidence, not always completely justified by its accomplishments. The reliance which is placed upon roentgen study often goes far beyond the merits of the method. The contrary, of course, is also true, so that some definition of its limitations should be attempted. I use the term limitations in its broad sense, that is, as meaning the maximal as well as the minimal possibilities.

That there are situations in which disease processes are present without any roentgen evidences of abnormality whatsoever is well known. Likewise that positive roentgen findings may become apparent at a stage in the development of an abnormal process when symptoms, physical signs or any other evidences whatsoever are completely lacking is also known. Despite this there is relatively little written on this subject in textbooks or in current periodicals. It is difficult to find adequate discussion concerning the real significance of the negative roentgenogram in various diseases.[4,27] While the details of such structures as the lungs or the skeleton appear to be faithfully reproduced in the roentgenogram, a correlation of anatomical and roentgen findings reveals that many lesions which are microscopically apparent give no roentgen findings. It is evident that lesions must attain a sufficient size or produce sufficient changes before they have enough contrast density to be visible. Brailsford[3] has pointed to the most obvious example, pregnancy, in which the process must be present for at least nine or ten weeks before there is any chance of roentgen diagnosis. Another example which is known to all and fully described in most textbooks is acute osteomyelitis. Here the absence of roentgenologic signs for as long as two weeks—if an antibiotic or chemotherapy has been given the period may be even longer—after the onset of symptoms is a notable feature of the disease. Conversely, by means of roentgen examination of the stomach we have been able to demonstrate tumors as small as 5 millimeters and as large as 7 centimeters in diameter in patients who have no symptoms whatever.

There are three points of reference which one might use in determining the value of the roentgen method in the detection of an abnormal state at its earliest beginnings. The first would be the time of the actual onset of the disease, whether it be the day or hour of exposure, in the case of an infectious process, or the time of implantation of the tumor in the case of a neoplasm. In the former there is some possibility of determining this point of reference, particularly in such diseases as tuberculosis in which a specific exposure can often be clearly ascertained. In the case of neoplasms in humans it is impossible to state with any degree of certainty the exact time of inception. When such information is not available, as is the case in many lesions, another point of reference must be used, namely, the time of onset of symptoms. A third method of judgment rests in a quantitative determination of the size of the lesion necessary to be demonstrable by roentgen study.

To illustrate a method of procedure which should lead to a better understanding of the

limitations of roentgen diagnosis, I wish to present some data which we have collected concerning diseases of the thorax, data derived from experimentation, from case study, and from what might be called the past roentgen history. I hope to discuss briefly pulmonary edema, pleural effusion, pneumonia, chronic tuberculosis, acute miliary tuberculosis, metastasis to the lungs and, finally, bronchogenic carcinoma, from the point of view of the possibilities of roentgen diagnosis.

The rationale of this approach is based somewhat on the following experiences which, I believe, any roentgenologist is likely to encounter. A student discovers that the sputum of a patient whom he has examined contains a great number of tubercle bacilli. Characteristically, the student promptly appears in the Roentgen Department to have a roentgen examination of his chest and he wants to know at once whether or not he has tuberculosis. What answer should be given if his roentgenogram is negative? A patient comes into the hospital with high fever, leukocytosis and all of the symptoms of pneumonia. There are no physical signs. A roentgenogram is made, it appears to be negative, and the intern comes to ask, "Well, what does this mean? Does this patient have pneumonia even though the roentgenogram is negative?" A patient comes in with a very acute fever of perhaps a week's duration. He has cyanosis and tachypnea; the diagnosis of acute miliary tuberculosis is entertained because of his condition. Roentgen examination is made and the film appears to be entirely negative. What shall we say as to the diagnosis at this time or what criteria do we have for establishing the reliability of the roentgen study under such circumstances?

PULMONARY EDEMA

Many pulmonary lesions may well be classified into two categories: those which predominantly affect the alveoli and those which are essentially interstitial. The roentgen findings are usually obvious at an early stage in the alveolar type of lesion and are readily observed even when the findings are minimal. The converse is true of the interstitial processes which present recognizable changes in the roentgenogram only after complete development of the process. Pulmonary edema of ordinary clinical significance is usually a process in which there is exudation of fluid into the alveoli as a result of cardiac failure, overloading of the circulation, hypoproteinemia, renal failure, as well as many other conditions. There is, however, also an interstitial edema which seems to be associated with inflammatory processes and, curiously enough, seems to occur in animals as a result of circulatory failure. The difference in the time of appearance of roentgen findings noted above is true of these two types of edema as well as in the two types of inflammatory processes.

We have had occasion to study a large number of patients developing pulmonary edema either postoperatively[19] as a result of overloading of the circulation during a period in which the myocardial capacity is somewhat impaired or in the usual medical conditions. We have learned that this type of pulmonary edema can be demonstrated quite effectively on the roentgenogram at a time when the symptoms are minor or difficult to interpret and the physical findings are either minimal or completely absent.

To illustrate, the following 2 cases are reported because they demonstrate how rapidly changes may appear in a roentgenogram of the lung, and how sensitive the roentgenogram is as an indicator of the presence of fluid in the alveoli.

Case 1. A patient with glomerulonephritis had had a period of hypoproteinemia accompanied by generalized anasarca, extensive pulmonary edema and pleural effusion. She had recovered completely from this attack, the roentgenogram of the lungs was entirely clear; there were no physical findings whatsoever and the peripheral edema had disappeared completely. She was about to be discharged from the hospital when the intern came in to see

her and she complained that she did not feel quite as well as she had the day before. There was a slight increase in her respiratory rate but little else was obvious. She had been seen early that morning and appeared quite normal. The physical findings were entirely negative. Within two hours of the first onset of this slight dyspnea, a roentgenogram of the chest was made and showed definite edema in the lungs as manifested by the usual mottling and increased density along the vascular trunks. Within another six hours the changes were more prominent and the full blown picture of typical pulmonary edema appeared.

An even more striking illustration of the roentgen demonstration of edema is illustrated by the following case report.

CASE II. A patient with Addison's disease was being studied by Dr. Gerald Evans and his associates concerning the effects of the administration of desoxycorticosterone acetate and high salt intake upon the size of the heart. Roentgenograms of the chest were being made at frequent intervals with a view to determining the relative changes in cardiac size. During the course of these examinations this patients showed in addition to the tuberculosis of the adrenals, that there was an actual tuberculosis of the lung. The heart was very small, the lungs were dry and anemic looking, during the periods of addisonian crisis. There were several periods of treatment during which salt and desoxycorticosterone acetate were given and then withdrawn. On one of these occasions when a roentgenogram of the heart was made at a time when there were no symptoms nor physical signs whatever to suggest any abnormality in the lungs, clear evidences of pulmonary edema in the bases of the lungs were apparent (Fig. 1). The findings were so suggestive that the attention of the clinicians was directed to it at once. Even after looking at the roentgenogram and being given the opinion that pulmonary edema was present they re-examined her lungs, with negative results. There were, likewise, no evidences whatever of subcutaneous edema. A review of the careful studies of the blood volume, which were being made daily, indicated that on this day a striking dilution of the blood with retention of chlorides was present, so much so that pulmonary edema might readily have resulted.



FIG. 1. Case II. Pulmonary edema, early stage. The roentgen findings of streaked mottled, diffuse density at both bases were present before the appearance of obvious symptoms or physical signs. The presence of edema was confirmed by the laboratory findings.

Comment. Both of these cases demonstrate how sensitive the roentgen examination is as an indicator of the presence of pulmonary edema.

Another illustration to demonstrate the early evidences of pulmonary edema in the roentgenogram is afforded in patients who are having surgery on the thorax and who are not infrequently put in various positions in which the circulation to the lung is greatly hampered. Under such circumstances edema of one lobe or one lung may readily develop. We have made roentgen studies on the operating table of a number of such cases in which some suspicion appeared in the mind of the surgeon because of the behavior of the patient that edema or atelectasis might be taking place and we have been able to demonstrate the findings of edema in the dependent lobe within a few minutes after it occurred.

In experiments made on goats by Nessa and myself we attempted to demonstrate the earliest stage in which edema could be clearly delineated in the roentgenogram. The animals were put in the supine position which was throught would result in severe

circulatory failure. Pulmonary edema was thought to occur early. We were chagrined to find that roentgenograms did not reveal the kind of changes we have learned to expect in edema and only late in the course of the process did some findings appear. These were difficult to interpret and were certainly not at all characteristic of our findings in pulmonary edema. However, on microscopic examination of the lungs in these animals we found that they did not develop fluid in the alveoli, the kind of pulmonary edema we are accustomed to seeing in cardiac failure, but rather fluid and infiltration in the interstitial tissues. Under such circumstances it appears that the roentgen findings are much less characteristic, far more difficult to interpret, and appear at a much later stage in the process.

PLEURAL EFFUSION

The sensitivity of the roentgen method for the demonstration of fluid in the thoracic cavity is well shown in patients with pleural effusion. In the case of transudation the point of reference must be quantitative rather than one of time since it is impossible to determine in most instances either from symptoms or from other evidence as to exactly when the transudate began to accumulate. In the case of exudates there are usually symptoms which give a point of reference.

Experiments with monkeys, performed by one of my associates in connection with some other work on pleural effusions, in which various fluids were introduced into the pleural cavity in known amounts, were recalculated on the basis of the relative volume of the thorax of the animals under consideration and that of the average adult. As a result of this it appears probable that a minimum of 100 cc. of fluid in one hemithorax of the average adult is required for demonstration by roentgen study and then can only be seen if the lateral decubitus position is used. By using the lateral decubitus position, in clinical cases, we have been able to demonstrate very small quantities of fluid repeatedly, when physical findings were absent, as previously reported.[23,24] On the other hand, if reliance is placed upon the usual upright film made in deep inspiration, fluid may not be apparent in the roentgen study when there are already some physical findings. Under such circumstances the quantity of fluid must reach 300 to 400 cc. before there are roentgen changes. Another indication of the presence of small quantities of fluid lies in the appearance of the shadow of the interlobar fissure when the position of the patient is changed from upright to supine or prone. This is, of course, particularly true on the right side.[25]

PNEUMONIA

In the case of pneumonia it is rather difficult, of course, to establish the exact time when the infection occurred, at least in terms of hours. We can, however, in a few cases get a point of reference from the symptoms of the patient. This is, of course, particularly true of the bacterial pneumonias, the so-called lobar pneumonias, in which not uncommonly, the onset is sudden and sharp. We have made some efforts to obtain roentgenograms on patients very shortly after their first complaint. In many cases, because of a special combination of events, we have been fortunate in securing films on patients with pneumonia at a far earlier stage in the course of the disease than commonly happens.

It should be noted that the demonstration of consolidation in the lung is attended by many sources of error. Lateral views are often necessary[31] and particularly is it important to observe the density of the cardiac shadow.[26] The reports in the literature reflecting on the absence of roentgen findings when pneumonia is actually present are often the result of poor observations, especially the failure to take the above points into consideration. To illustrate the possibilities of early roentgen diagnosis in bacterial pneumonia, the following 2 cases will serve.

Case III. A male presented himself with the following clear-cut history. He said he was

perfectly well until a sudden onset of chills and fever and pain in the chest brought him to the hospital. The onset was very sharp and his history appeared to be very reliable. A roentgen examination (Fig. 2) was made one and a half hours after the first symptoms and already a triangular shadow of increased density, streaked in appearance and very characteristic of the very early stage of so-called lobar or bacterial pneumonia, is apparent in the right upper lobe.



FIG. 2. Case III. Lobar pneumonia, one and a half hours after onset. The roughly triangular area of increased density in the right upper lobe exhibiting characteristic linear and homogeneous shadows is typical of lobar pneumonia in the early stages. Twenty-four hours later the entire lobe was densely consolidated.

Twenty-four hours later the process became extremely dense, went on to involve the entire lobe in perfectly characteristic fashion and the more typical appearance of lobar pneumonia was found. This was a pneumococcus type pneumonia.

CASE IV. A child was coming to our outpatient clinic for another condition. He was seen late in the afternoon, his temperature was taken and various other examinations were done and at that time he was apparently perfectly normal. He had to remain over for further examination the next day so he went to a motion picture theater that evening where he suddenly was taken with severe pain in the side, began to cough, and felt very uncomfortable. This persisted so that he had to leave the theater and finally reported to our admissions department. A roentgen examination was made at once, just two and a half hours after the very first symptom. Here again, in the lateral view, the triangle of streaked density which is so typical of early lobar pneumonia was found.

Thus we see that in 2 cases of bacterial pneumonia an hour and a half and two and a half hours after the first onset of symptoms, diagnostic roentgenograms were apparent. In our experience in such cases some physical signs also appear very soon after the appearance of roentgen signs. We have studied some 20 fairly well controlled cases of similar character and it is our impression that practically all cases of bacterial pneumonia of the ordinary type will give positive roentgen signs within twelve hours and in the majority of cases within six hours after the first onset of symptoms.

In the case of the atypical or virus pneumonias the situation is completely different and it is interesting to note that these are really interstitial processes at the beginning whereas the bacterial pneumonias start with an intra-alveolar exudation. The difference in the pathologic findings likewise produces a sharp change in the time of development of roentgen findings. In atypical pneumonia twenty-four and even forty-eight hours may elapse before one can make a definite determination of an abnormal process in the roentgenogram, although the patient's symptoms are outstanding. The physical findings are even slower in their appearance and the roentgen findings almost always precede the physical signs. There are, of course, cases in which the roentgen findings are readily apparent although the patient has very few symptoms. But when the time of onset is known, it will be usually found that a fairly long period has elapsed before the roentgen findings appear.

CASE V. A white male, aged twenty-four, was admitted to the hospital one week after the onset of symptoms. The illness began with a chill and there had been daily temperature elevations as high as 102° F. Persistent cough with expectoration of mucopurulent sputum was present. There were a few crackling rales

over the right lower lobe. The white blood count was 11,000 with 81 per cent neutrophiles. The sputum showed only micrococci and staphyloccoci. Later studies of the sputum, the reaction to therapy and the temperature curve all suggested a fairly characteristic picture of atypical pneumonia. On roentgen examination, however, only a few faint changes were made out in the lower lobes which were rather difficult to interpret. They may well represent interstitial infiltrations, but are not at all characteristic.

Comment. This is an example of an atypical pneumonia present for almost a week yet giving roentgen findings which might well be considered essentially negative.

A negative roentgenogram, therefore, twelve hours after the onset of symptoms suggesting lobar pneumonia is of great significance. In patients with symptoms of atypical pneumonia, however, forty-eight hours must elapse before negative findings can be considered at all conclusive.

CHRONIC TUBERCULOSIS

Many years ago McPhedran[14] and Opie[20,21] directed attention to the latent period which usually elapses between the appearance of the roentgen signs of pulmonary tuberculosis and the development of symptoms. In 1934, we[29] used the term "latent period" to designate the delay between the exposure to the tuberculous infection and the development of roentgen findings. We reported a series of 5 cases of pulmonary tuberculosis in young adults whom we had the opportunity to observe frequently and whose history of exposure and tuberculin skin test was known. Recently there have appeared an editorial[4] and papers[3,5] by Brailsford in which he likewise directs attention to this latent period between the beginning of a disease and the development of roentgen signs. Brailsford also emphasizes tuberculosis since it is of considerable importance to know the significance of negative roentgen findings in relationship to the time exposure due to tuberculosis. That some delay must occur is evident. Such an interval may account, in part at least, for the failure to sift out all cases of tuberculosis in induction centers, for example, or in tuberculosis surveys.

We have now collected 13 cases in which we have been able to ascertain data similar to those previously reported. In these patients negative skin tuberculin tests and negative roentgenograms are on record on repeated occasions. The time of exposure to a known case of tuberculosis is fairly clear. From three to five weeks after the exposure there is a conversion of the tuberculin test from negative to positive. In some cases we have roentgenograms made four, five and six weeks after the tuberculous exposure with negative results. Then at ten to twenty weeks positive roentgen findings appear and further study for a number of years confirms the diagnosis of tuberculosis.

It should be noted that these cases are of a particular character since they are young adults apparently tuberculosis free before exposure, yet the roentgen findings suggest what is usually designated as reinfection tuberculosis. I should emphasize that none of these patients had symptoms at the time of the discovery of the lesion although they developed symptoms later. An illustrative case of this type is described below.

Case VI. A nurse, aged nineteen, had been examined several times. Her tuberculin skin test was negative and the roentgenograms of the chest were negative. She was exposed to tuberculosis in a group of patients. Five weeks later, her tuberculin skin test was found to be positive. At the same time the roentgen examination was negative (Fig. 3*A*). Ten weeks after exposure a small area of infiltration measuring about 10 mm. in diameter appeared in the left subclavicular area (Fig. 3*B*). There was some evidence of exudation about it. There were no clinical symptoms nor physical signs. Five months later the lesion showed some diminution in size and appeared denser and more fibrotic. The shadow remained about the same thereafter.

It is interesting to note that Malmros and Hedvall,[11] in a monograph on the development of tuberculosis published in 1938, were able to collect a series of somewhat similar cases and in their group they

undoubtedly have been able to demonstrate, in a few cases at least, roentgen findings eight weeks after the first exposure to tuberculosis. The latent period, here described, is no doubt dependent upon the size of the lesion and it is significant that there is a close correlation with the experimental work on tuberculosis in animals. It takes about six weeks after the usual type of induction of experimental chronic tuberculosis in animals for tubercles to coalesce in characteristic fashion. Obviously some further time has to elapse before these microscopic tubercles enlarge sufficiently to arrive at a size of nodule which is demonstrable on the roentgenogram.

Dale[7] has reviewed the whole subject of the visibility of small lesions in the lung in great detail, particularly with reference to early tuberculosis and miliary tuberculosis. McPhedran,[12,13] and a great many others, have done many experiments in an effort to demonstrate what size a single lesion must attain to be visible in the roentgenogram of the adult chest. McPhedran[13] showed that lesions of 1.5 to 2.0 millimeters in diameter could be demonstrated in the inflated lung removed from the thorax. McPhedran and Weyl[15] have indicated some of the technical factors involved in the demonstration of small tuberculous lesions. Morgan[16,17,18] has recently reviewed the technical factors in the demonstration of small shadows. Experiments which Dr. Joseph Jorgens has been conducting on living individuals under favorable technical conditions and also with the use of a phantom have up to this time indicated our inability to satisfactorily demonstrate a single lesion in the living individual less than 3 millimeters in diameter. In the phantom 2 millimeters appears to be the minimum. Further experiments are being carried in on this direction.

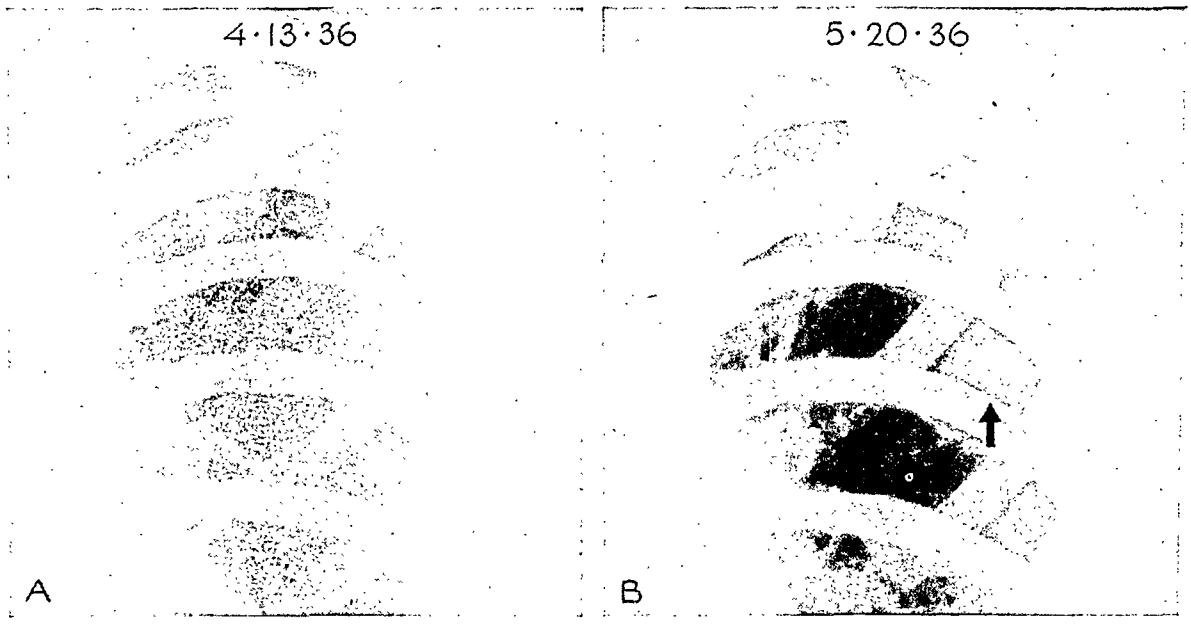


FIG. 3. Case VI. Pulmonary tuberculosis with early roentgen findings. *A*, roentgenogram, left upper lobe, made five weeks after exposure to tuberculosis, immediately after conversion of tuberculin skin test to positive. The area appears entirely normal. *B*, roentgenogram of same area five weeks later and ten weeks after exposure to tuberculosis. Typical findings (arrow) indicative of tuberculosis are shown. The shadow was reduced in size and gave a more fibrotic and nodular appearance in roentgenograms made five months later.

ACUTE MILIARY TUBERCULOSIS

In connection with this, the matter of acute miliary tuberculosis is of great importance. I believe every experienced roent-

genologist and phthisiologist would agree, with only very minor exceptions, that individuals who have symptoms which are the result of chronic parenchymal pulmonary tuberculosis will exhibit demonstrable roentgen signs. Patients with symptoms usually have sufficient exudation so that the roentgen examination is positive. There are some exceptions, of course, to this rule. In most cases, the exceptions, I believe, will be found to be, not the usual parenchymal tuberculosis, but rather bronchial tuberculosis in the early stages before there is appreciable parenchymal extension or bronchostenosis. In such situations, i.e., a pure bronchial tuberculosis, symptoms such as hemoptysis may be present, the sputum may contain tubercle bacilli without definite roentgen findings being exhibited. This might well be expected from the anatomy of the process.

In the acute pulmonary tuberculous processes, particularly acute miliary tuberculosis, the dictum that roentgen findings precede symptoms does not hold. In a large percentage of the cases of acute miliary tuberculosis the roentgen findings are completely absent at the first onset of symptoms and often for a long period of time thereafter.[1,7,9,8]. So far as we can determine from correlated studies of autopsies and roentgen examinations the difference lies largely in the number and size of the tubercles which are present.[22] When one considers that the usual miliary tubercle is less than 1 millimeter in diameter it becomes evident at once that some other factor must be present in order to give the striking picture which acute miliary tuberculosis frequently exhibits. This additional factor has been the subject of a good deal of discussion but it seems to me it has been fairly well established that it is largely a matter of superimposition. If a sufficient number of these small 0.5 or 1 millimeter sized tubercles are lined up, a sufficient density will be produced to give the shadow which is seen in the roentgenogram and until that time the roentgenogram may appear to be completely negative.

In some cases striking and characteristic findings will appear within a week or ten days after the onset of symptoms. In many, however, as long as six or eight weeks may elapse. The following case demonstrates the latter finding.

Case vii. A patient who had a mass in the mediastinum, which was thought to be a dermoid cyst, was admitted to the hospital and was operated upon. The cyst was found but owing to inflammatory adhesions could not be entirely removed, so was drained. Shortly thereafter she developed a fever which rapidly became severe, dyspnea developed and seven weeks later she died. Roentgen examination of the chest was made on several occasions, the last being six days before death, and the appearance was normal except for the tube draining the mediastinum. At autopsy, numerous miliary tubercles measuring from 0.5 to 1 mm. and a few 2 mm. in size were found. These were largely on the pleura and were rather widely, but thinly, distributed. There were some in the lungs as well. The number was much less than is usually the case and I am inclined to believe that this is the explanation for the failure to observe any changes on the roentgenogram.

Comment. Six weeks after the first ontse of symptoms of miliary tuberculosis, a satisfactory roentgenogram of the chest failed to reveal any evidence of the disease. We have seen many other cases of the same type. A negative roentgenogram, therefore, even six weeks after the onset of severe symptoms, does not exclude acute miliary tuberculosis. Roentgen findings may be present but frequently are not.

METASTASIS TO THE LUNGS

That very small lesions in the lungs can be demonstrated effectively by roentgenography is best shown in the case of metastatic processes particularly such as occur from sarcoma, from Ewing's tumor and also, in all probability, from carcinoma. We have been able to observe a number of such cases and to have the opportunity to demonstrate the difficulties and the advantages of roentgen examination in this situation. Here we have a condition in which the roentgen findings invariably pre-

cede the symptoms and the physical signs; they certainly appear at a very early stage in the development of the lesion. It is, of course, impossible to say when the lesion actually began. Brailsford[5] has said that he could demonstrate metastases from sarcoma within two weeks of their dissemination but he has made the assumption that the dissemination occurred on the day of amputation, an assumption which is scarcely valid. We have studied a number of such cases intensively and I should like to report one of these to illustrate our observations.

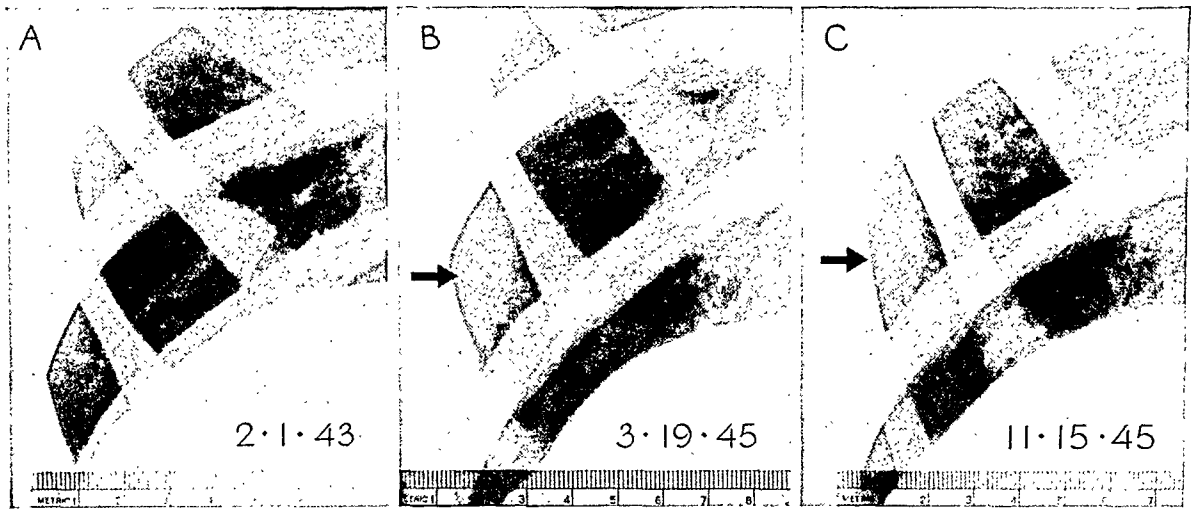


FIG. 4. Case VIII. Metastasis to lung from Ewing's tumor. *A*, roentgenogram, segment of right lower lobe, made at time of amputation. Normal. *B*, same segment about two years later. Note small nodule measuring 3 mm. in diameter clearly visible. This approaches the minimum size permitting roentgenographic detection. *C*, same segment eight months later. Note increase in size of metastatic nodule which now measures 7 mm. in diameter.

CASE VIII. A male, aged fifteen, developed a Ewing's sarcoma of the tibia; amputation was done and it was followed by irradiation. His lungs were being examined at semi-annual intervals with a view to finding metastasis. The roentgenograms (Fig. 4*A*) appeared entirely normal until about two years after amputation when the first change was observed; that is, an extremely small nodule measuring about 3 mm. in diameter in the roentgenogram was seen (Fig. 4*B*). It was clearly visible because of its location well out at the periphery of the lung where the contrast with the surroundings was striking. This being the only lesion in the lungs we were in some doubt, naturally, as to the exact diagnosis, although it was felt that a metastasis was probably present. Eight months were allowed to intervene before a re-examination was done and at the end of that time the lesion appeared to have grown in size so that now it measured about 7 mm. in diameter (Fig. 4*C*). At this time since no other lesion could be found, a segmental pneumonectomy was performed by Dr. John Paine and Dr. Richard Varco. The specimen showed a typical metastatic nodule actually measuring about 6 mm. The patient recovered promptly and without incident. He was re-examined again about seven months later. The lesion on the right was entirely absent and there were no residual evidences of the surgery, but now a similar nodule became apparent on the opposite side. It was not clearly recognized at this time, but on re-examination six months later it was observed. At this time a segmental pneumonectomy was performed on the left and a similar tumor removed. There was already another metastasis on the right but it was so small that it was not observed. Six months later several metastases became clearly evident. The differentiation of such small lesions from vascular shadows is difficult but may be accomplished by making films in different phases of respiration, by rotation, or by timing the exposures in the cardiac cycle as described by McPhedran and Weyl.[15]

Comment. It is evident that in the case of metastasis exceedingly small lesions may be seen before there are any symptoms or physical signs.

There is, however, even here, another side of the question not commonly pointed out and that is the case of miliary metastases in which the lesions are less than 1 millimeter in size. If one follows patients to autopsy consistently, it is astonishing occasionally to find a patient whose pleural surfaces appear to be studded with tiny metastases yet the roentgenograms appeared to be entirely negative. A characteristic example is reported below.

Case IX. A patient with carcinoma of the esophagus was operated upon by Dr. Richard Varco. During the course of the exploration of the mediastinum he also explored the left lung and found numerous, exceedingly small miliary nodules over its surface. These were confirmed first by biopsy and later at autopsy as metastases from carcinoma. Yet a roentgen examination had been made the day before operation and nothing was seen but a few tiny shadows; they were indistinguishable from the vascular trunks. Even knowing the findings it is impossible by magnification or otherwise to demonstrate any abnormal shadows.

Comment. It is clear that metastases of 3 millimeters or over may often, although not always, be shown on the roentgenogram. Miliary metastases, like miliary tubercles, may readily escape detection.

BRONCHOGENIC CARCINOMA

Finally, with this same point of view in mind, I should like to explore one more field of roentgen diagnostic endeavor; that is, primary carcinoma of the lung. Here again we have no means for determining the time of onset but we do have evidence with regard to the first symptoms of the patient. The problem of whether or not we can determine the presence of a primary tumor in the lung by means of roentgen examination prior to the onset of symptoms is of considerable importance. The widespread trend toward mass surveys of the chest may well lead us in the direction of an attempt to diagnose such tumors in symptomless individuals more frequently than heretofore.

Because roentgenograms of the chest are made so commonly we have been successful in finding earlier films made in various institutions other than our own on a considerable number of patients in whom we have suspected or have demonstrated the presence of a bronchogenic tumor. We have thus obtained a sort of past roentgenologic history that has permitted us to get some idea as to whether or not carcinoma of the bronchus may be present with symptoms and without apparent roentgen findings or, conversely, whether the roentgen findings may appear in many cases before the onset of any symptoms whatever. Our experience in a number of cases indicates: (1) that with adequate examination the roentgen findings may well be evident in many cases at a time when the patient is apparently well; (2) that the roentgenologic findings are almost always present if the patient has symptoms; (3) that the cases in which physical signs and symptoms are present while there appears to be an absence of roentgen findings, adequate examination, particularly in different phases of respiration, will almost invariably produce roentgen evidences of abnormality.

In order that abnormal changes be observed in the early stages which we are considering, it is necessary to pay close attention to relatively minor changes in the normal lung pattern. Particularly is it necessary to determine differences in the degree of inflation of the lungs during the phases of respiration. I do not wish to go into the details of the roentgenologic findings in primary tumors of the lung. I would only point out three important signs which are exhibited in this series of roentgenograms, to which perhaps more attention should be given. Let me emphasize that none of the things that I shall speak of are necessarily pathognomonic of bronchogenic carcinoma. They represent, however, clues which should lead us to further

investigation and thereby the establishment of the diagnosis in more unequivocal fashion.

The first sign is enlargement of one of the root shadows of the lung. We all appreciate the great variation which exists in the size of the root shadows and the numerous lesions which may produce enlargement of one or both of the root shadows, leaving it as a residual but without present clinical significance. Nevertheless, in view of the increasing frequency with which carcinoma of the lung is seen and the extreme importance of the problem from the standpoint of the saving of many individuals it is incumbent upon us to give more attention to such minor changes.

CASE X. A patient came with pain in the fibula which proved to be due to a destructive tumor. On biopsy examination this was shown to be a metastatic adenocarcinoma. Routine examination of the chest (Fig. 5*A*) was then made and an enlarged root shadow on the right side was found. On the lateral view (Fig. 5*B*) this was clearly in the center of the lung around the bronchi. Further studies with bronchography and planigraphy revealed constriction of the right lower lobe bronchus characteristic of carcinoma. The lesion might well have been completely overlooked had it not been for the metastatic process which was already present. The patient had no pulmonary symptoms. (Previously reported.[19])

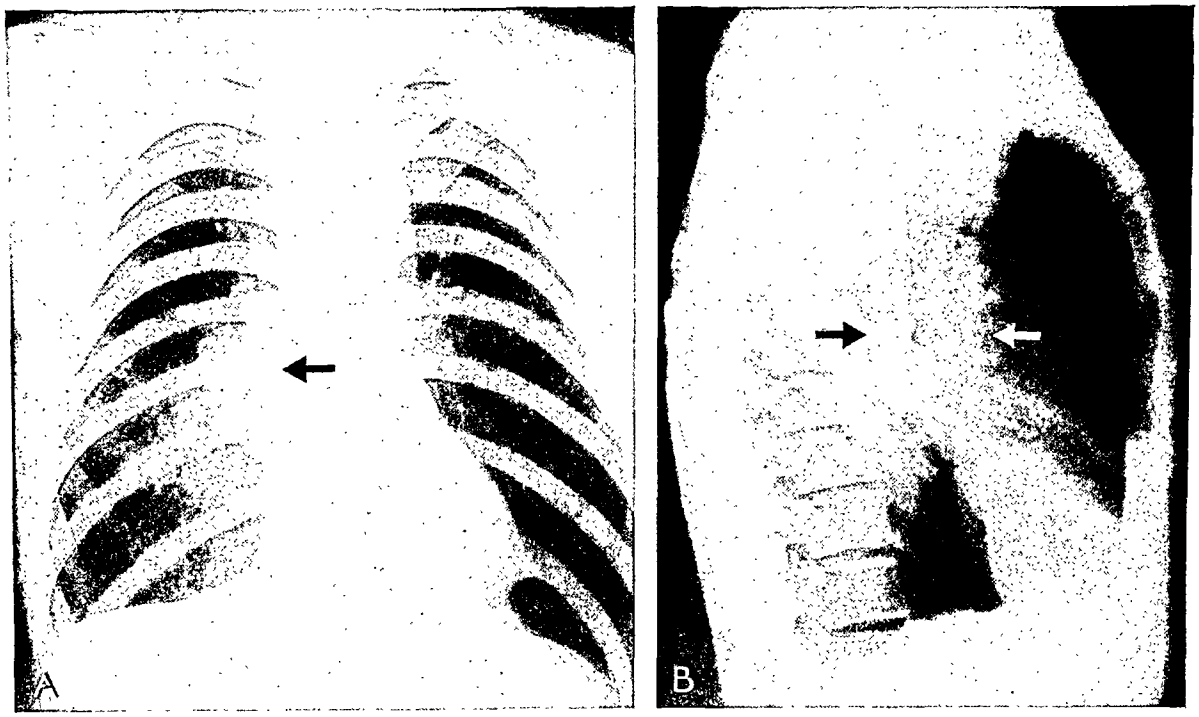


FIG. 5. Case X. Primary carcinoma, right lower lobe bronchus, without pulmonary symptoms found on routine examination. *A*, posteroanterior roentgenogram. Note enlargement of right hilar shadow (arrow). *B*, right lateral view. The enlargement of the root of the right lung with irregular radiating borders is well shown (arrows). There is a generalized emphysema of independent origin.

Comment. Unilateral enlargement of the hilar shadow in a symptomless individual might well be observed during the course of a mass survey and such cases should certainly be singled out for intensive study.

The second sign is an area of density in the periphery of the lung which may be round and sharply defined or irregular and poorly defined. In themselves such isolated shadows are difficult to distinguish from a variety of other processes such as tuberculoma, atypical pneumonia, benign tumors, localized abscesses or fluid-filled cysts. Nevertheless such a shadow may be the

first clue to the presence of a peripheral or infiltrating carcinoma of the lung and is often found accidentally. The significance of the peripheral nodule as an early sign of carcinoma of the lung in symptomless individuals has already been thoroughly explored.[2,10] I would call attention to other types of peripheral infiltration which are not so obvious. The following 2 cases illustrate minimal findings in the periphery of the lung, representing the first stages of carcinoma; they may be detectable in the roentgenogram before the onset of symptoms or may readily be overlooked even after the development of symptoms.

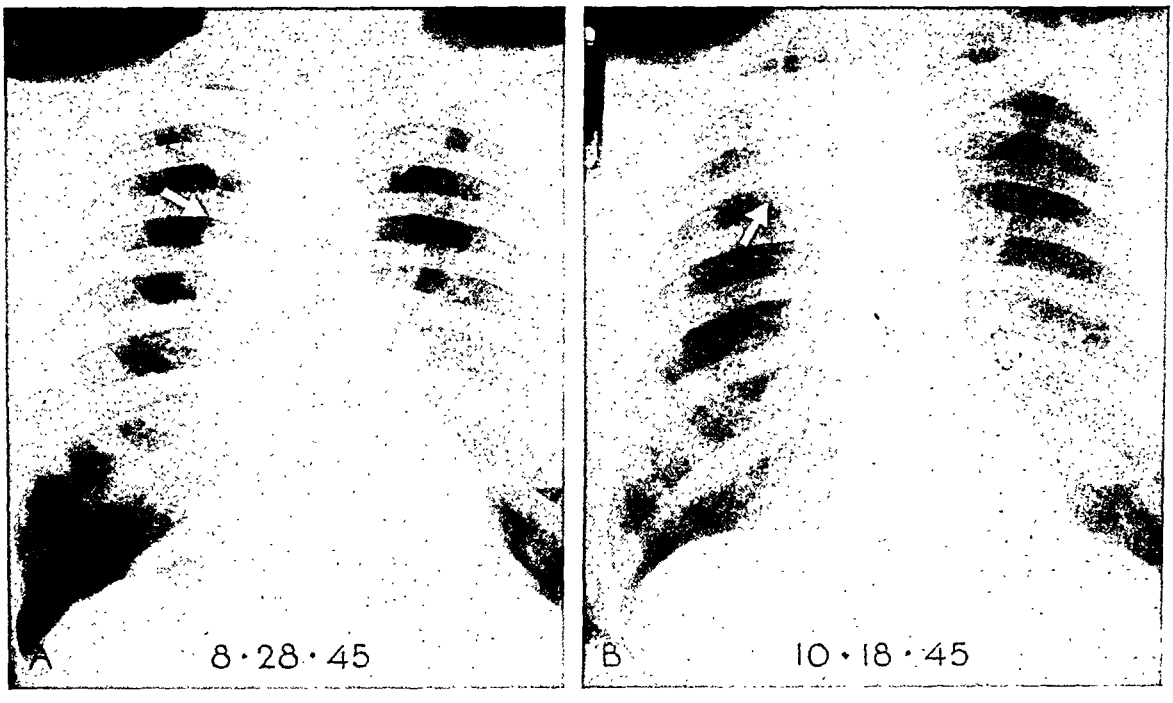


FIG. 6. Case XI. Bronchogenic carcinoma right upper lobe with symptoms and minimal roentgen findings. *A*, roentgenogram of right upper lobe, August 28, 1945, originally interpreted as negative. Note the very small nodule (arrow), the only evidence of the tumor at this time. *B*, re-examination of same area five weeks later. The lesion has grown in size and shows a fairly characteristic infiltration (arrow). (Courtesy of Dr. M. B. Hanson and Dr. Leo Nash.)

CASE XI. A male, aged fifty-nine, consulted a physician in July, 1945, when he began to complain of respiratory symptoms. There was a cough productive of a whitish to yellow sputum and a low grade pain in the chest, localized over the sternum, accompanied by weakness, fatigability and listlessness. Roentgenograms of the chest were made elsewhere on August 28, 1945, and were considered to be negative (Fig. 6*A*). On re-examination, however, there is shown a very small density in the right superior mediastinum with slight enlargement of the hilar shadow. Because of the negative diagnosis nothing was done; the pain continued and became somewhat more severe. He was admitted to another hospital on September 29, 1945, where he developed chills and fever and a diagnosis of atypical pneumonia was made. Roentgenograms made on October 1, 1945 (Fig. 6*B*), show a definite infiltration of considerable degree in the right upper lobe extending out from the mass which was originally present in the films of August 28.

He was first seen here October 21, 1945, at which time he was seriously ill and a mass had developed overlying the sternum between the third and fourth interspaces on the right side. There were no physical findings so far as the lungs themselves were concerned, except for some dullness over the area of the mass. Bronchography was undertaken and no obstruction to the major bronchi could be made out. It was impossible to fill out the anterior branches of

the right upper lobe bronchus, however. Further examination showed destruction of the sternum and a mass extending to the left side.

The patient died on November 7, 1945. In the right upper lobe numerous nodules varying in size from 1 to 5 by 4 mm. in diameter were found. In addition there was a large lobulated lymph node measuring 8 by 5 cm. to the right and superior to the bifurcation of the trachea. In the microscopic section these appeared to be typical of small cell carcinoma characteristic of a primary lung tumor. Metastatic lesions were also found in the sternum, spleen, kidney and brain.

Comment. Here we see a lesion, present in the roentgenograms made after the onset of symptoms, but unrecognized because of its extremely small size. When it became large enough to give a more definite shadow metastases had already occurred. It is evident that primary carcinoma of the lung may, in some cases, give respiratory symptoms even when the tumor is of small size and difficult to detect in the roentgenogram; yet the demonstration of the nodule in the original roentgenograms bears out the dictum that roentgen findings will be visible if symptoms are present.

CASE XII. A white male, aged sixty-two, was first seen in this hospital in October, 1938.He came in complaining of headaches, and a maxillary sinusitis was found to account for this symptom. A routine film of the chest was made at that time and was reported to be negative. However, on re-examination, minor changes suggesting fibrosis and infiltration can definitely be made out in the right apex. There were no pulmonary symptoms at that time although the changes in the roentgenogram are quite definite. Three months later he began to have some pain in the chest, slight cough with some fever. In February, 1939, clubbing of the fingers was observed by his own physician. Two weeks later another roentgenogram of the chest was made and a definite mass could be made out in the right apex corresponding to the areas of infiltration shown in the film made five months earlier. Later the process increased in size and the patient finally died as a result of the lesion, having developed metastases to the liver.

CASE XIII. A male, aged fifty-seven, came in because of pain in the chest and cough. On the first roentgenogram there was observed an area of emphysema in the right upper lobe. In the inferior portion of the right upper lobe there could be seen a somewhat linear zone of density fairly characteristic of atelectasis. The whole right upper lobe was larger than normal and on expiration failed to contract as did the remaining portions of the right lung and the left lung. Thus the combination of atelectasis and emphysema from obstruction of the right upper lobe bronchus was clearly observed in this case at this time. The posteroanterior roentgenogram made in expiration is illustrated in Figure 7*A*. Planigraphic and bronchographic examinations revealed a characteristic carcinomatous obstruction of the right upper lobe bronchus which was later proved by bronchoscopic biopsy. The bronchogram is shown in Figure 7*B*. At exploration the extent of the lesion was such as to make extirpation impossible.

Comment. The combination of atelectasis and emphysema produced simultaneously by a tumor of the bronchus is illustrated in Case XIII. In most patients the emphysema appears first; the atelectasis is a late development. In this case the symptoms were already present at the time the roentgen findings were observed.

CASE XIV. An iron miner was examined elsewhere on repeated occasions to detect early silicosis. He had some complaint of pain in the chest in 1944, and some cough prior to that time but this disappeared. He was seen January 29, 1945, at which time he had no complaints whatever. Routine examination of the chest was made because of the possibility of silicosis. In the roentgenogram made at this time elsewhere, a local area of emphysema in the right upper lobe can be made out characteristic of the segmental obstructive emphysema described by Westermark as the first sign of obstruction of the bronchus (Fig. 8*A*). It should be emphasized that there were no symptoms at this time. Several months later he began to have a cough and occasionally a little fever. Four months after this examination he developed a high temperature and an acute process from which he recovered very slowly. He returned to work in July, 1945. He continued to have slight cough. A year later, in July, 1946, routine examination of the chest was again made (Fig. 8*B*). At this time, however,

he had a chronic cough and some physical findings such as diminished breath sounds and dullness below the right clavicle. Later examination in this hospital revealed a characteristic atelectasis of the same segment of lung which was seen to be emphysematous in the roentgenogram made eighteen months earlier. Planigraphy and bronchography showed a characteristic carcinomatous obstruction of the right upper lobe bronchus which was later confirmed both by bronchoscopy and by exploration. The lesion could not be extirpated. (Case of Dr. R. W. Bray.)

Comment. In this case, then, a localized finding suggestive of carcinoma of the bronchus was present approximately two months before the very first symptom and eighteen months before any physical findings or serious symptoms were apparent.

Finally, I should like to report one more case which was somewhat complicated but illustrates again the possibility of early diagnosis of carcinoma of the lung prior to the onset of symptoms.

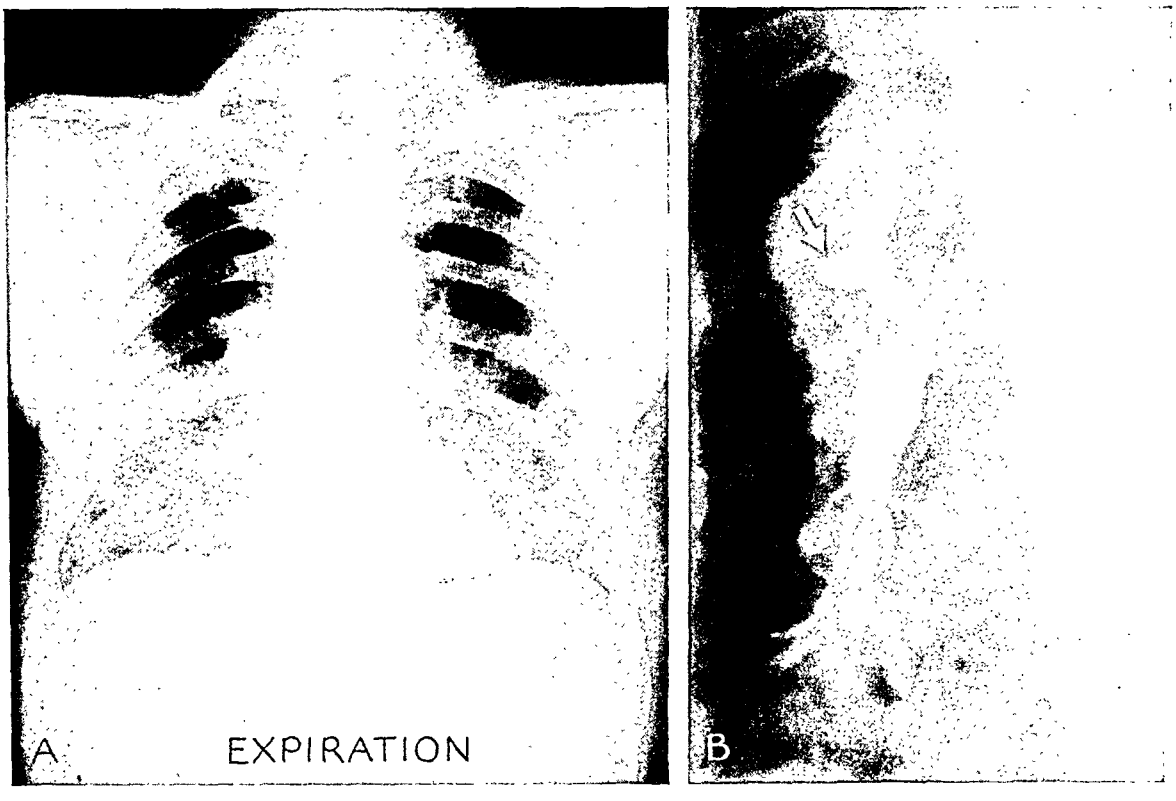


Fig. 7. Case xiii. Bronchogenic carcinoma with obstructive emphysema and atelectasis from the same obstruction. *A*, posteroanterior roentgenogram in expiration. Note the marked radiability of the upper portion of the right upper lobe in contrast to that of the opposite side and especially to the density of the lower portion of the lung. The latter shows the normal change resulting from expiration. In addition, there is a wide band of greatly increased density at the level of the horizontal fissure. The latter is in a low position although the diaphragm is elevated. There is therefore an obstructive emphysema of most of the upper lobe and atelectasis of its inferior portion. *B*, bronchogram made shortly thereafter. The characteristic carcinomatous obstruction of the right upper lobe is well shown (arrow). Note the appearance of complete obstruction despite the emphysema. This is probably owing to the fact that air may get into the lobe during coughing or straining while the viscous oil will not advance through so tiny an opening. The atelectasis below is the result of a more complete closure of that segmental bronchus. Planigrams made at the same time gave an identical picture of the tumor.

Case xv. A physician was known to have an enlarged right root shadow with calcification within it for many years. He was in the habit

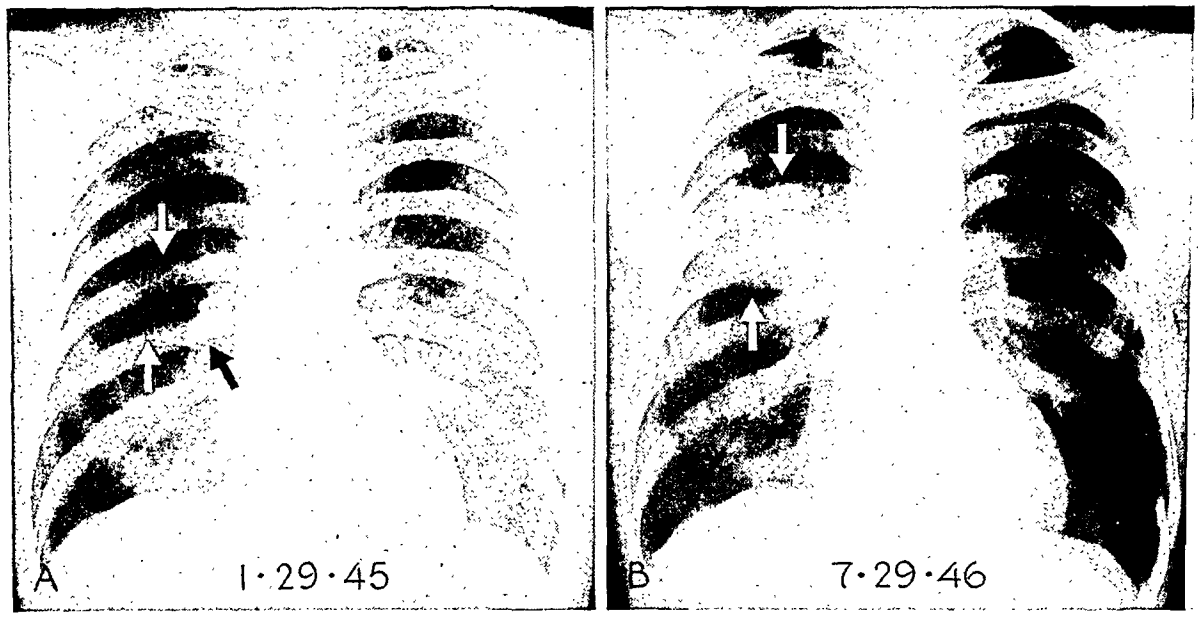


FIG. 8. Case XIV. Bronchogenic carcinoma showing segmental obstructive emphysema for over a year before onset of symptoms. *A*, posteroanterior roentgenogram in deep inspiration made as a routine procedure. Note slight increase in radiability of entire right lung with particular increase in segment of right upper lobe (arrows). There is a slight enlargement of the hilar shadow (arrow) of questionable significance. Roentgenograms made in the expiratory phase at this time would undoubtedly have exhibited the emphysema more effectively. *B*, re-examination eighteen months later, several months after the onset of symptoms. Note dense area of atelectasis (arrows) involving the same segment which was already emphysematous at earlier examination. The hilar shadow is definitely enlarged. (Courtesy of Dr. R. W. Bray.)

of having films of his chest made at yearly intervals because of this finding, although he had no specific symptoms. About two years before the development of any pulmonary symptoms he had a roentgen examination because he had a moderate hypertension and the determination of his heart size was desired. This examination was made at another hospital. A film was made in deep inspiration (Fig. 9*A*) and because the technician thought that this was an error, since the diaphragms were down too far, another film was made in mid respiration (Fig. 9*B*). It is interesting to observe the distinct difference between these two films at a time when this man had no symptoms whatever. There is clearly an obstructive emphysema of the right lung shown only in the expiratory film. He was re-examined approximately a year and a half later in deep inspiration only. At that time the first evidences, in addition to the obstructive emphysema, became apparent; that is, the root shadow had extended farther into the base of the lung and a nodule had appeared along its outer periphery. Unfortunately, because of the fact that the shadow had been large before and comparison was not made between this and the previous films, these findings were not observed. About three months later he coughed up a pea-sized broncholith. Two months later, he developed a dry cough accompanied by weakness, malaise and some dyspnea. Re-examination of the chest May 1, 1947, is illustrated in Figure 9*C*. A characteristic nodular tumor in the right hilum was seen and a diagnosis of carcinoma of the bronchus was made by Dr. J. R. Aurelius. Bronchoscopy on May 15 and May 22 revealed no findings so that the diagnosis was not accepted. About this time a few acid-fast bacilli were found in a smear from the sputum so he was sent to a tuberculosis sanatorium where he remained for some weeks. Finally on July 10, bronchoscopic biopsy revealed an undifferentiated carcinoma. Pneumonectomy was done but metastasis to the cervical lymph nodes was already present and he died some months later.

Comment. Minor changes in the lung indicative of emphysema might have been observed about two years prior to the onset of symptoms. Definite enlargement of the root shadow was present on roentgen

examination five months before the onset of symptoms. Such cases indicate unequivocally that in bronchogenic carcinoma positive roentgen signs may well be present before the first appearance of symptoms.

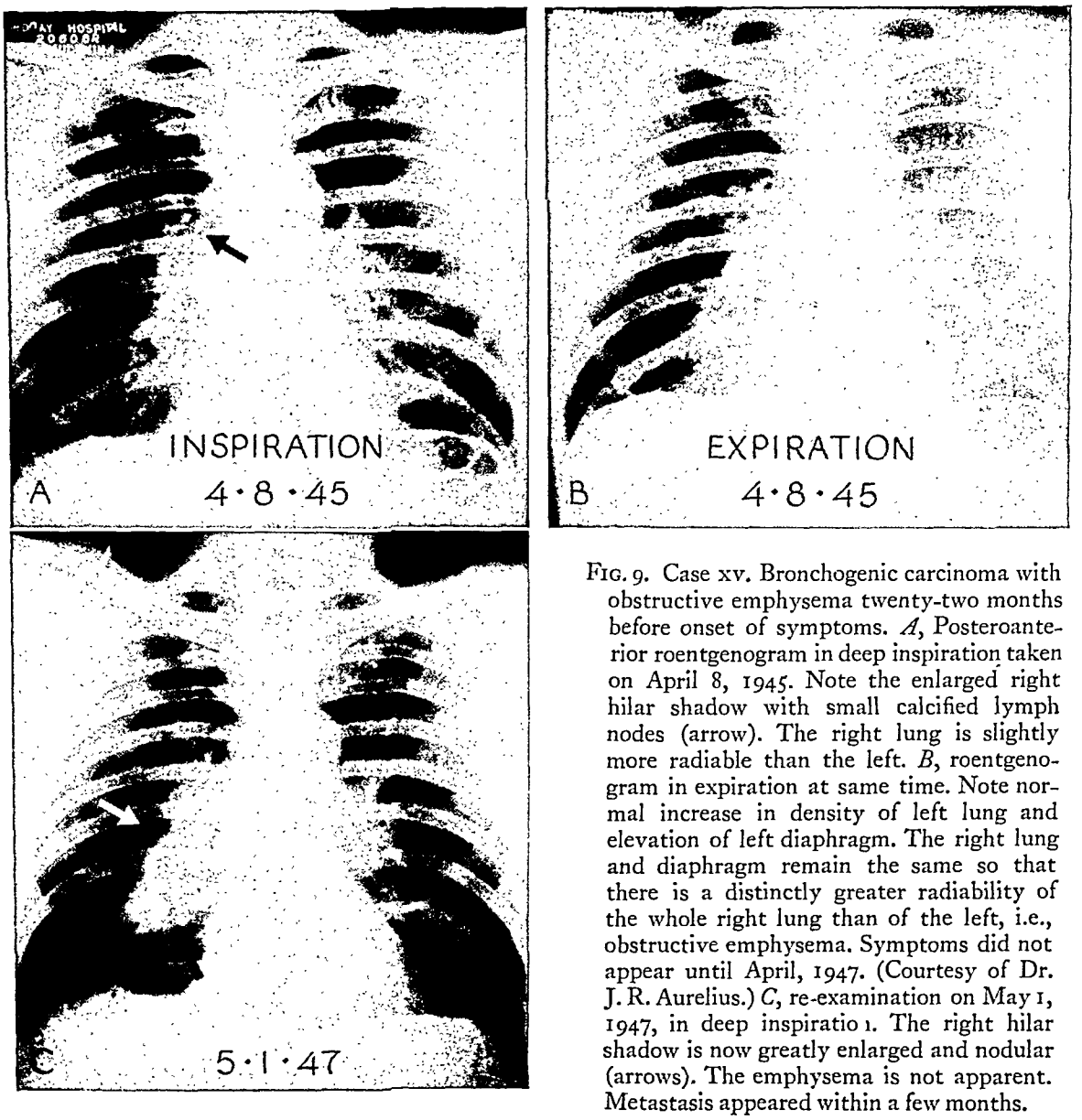


Fig. 9. Case xv. Bronchogenic carcinoma with obstructive emphysema twenty-two months before onset of symptoms. *A*, Posteroanterior roentgenogram in deep inspiration taken on April 8, 1945. Note the enlarged right hilar shadow with small calcified lymph nodes (arrow). The right lung is slightly more radiable than the left. *B*, roentgenogram in expiration at same time. Note normal increase in density of left lung and elevation of left diaphragm. The right lung and diaphragm remain the same so that there is a distinctly greater radiability of the whole right lung than of the left, i.e., obstructive emphysema. Symptoms did not appear until April, 1947. (Courtesy of Dr. J. R. Aurelius.) *C*, re-examination on May 1, 1947, in deep inspiratio 1. The right hilar shadow is now greatly enlarged and nodular (arrows). The emphysema is not apparent. Metastasis appeared within a few months.

SUMMARY

There are definite limitations to the roentgen demonstration of abnormalities. Some of these may be clearly defined and may be expressed in terms of the relationship of the appearance of roentgen signs to the inception of the disease or to the onset of symptoms or in a quantitative way. The possibilities and limitations of roentgen diagnosis are particularly well illustrated in diseases of the thorax. The results of some of our studies in this field are summarized as follows:

1. Pulmonary edema can be detected before the onset of appreciable symptoms and in the very earliest stage of its development, providing it is an intra-alveolar type of process.

2. Interstitial edema is poorly demon-

strated by roentgenologic examination.

3. Pleural effusion in amounts of 100 cubic centimeters or more can be detected if change in position of the patient is utilized during the examination.

4. Bacterial pneumonias are demonstrable, in some cases, within a few hours after the first onset of symptoms and in practically all cases within twelve hours after the first onset.

5. Atypical or virus pneumonias do not give distinctive roentgen manifestations for twenty-four to forty-eight hours after the onset of the symptoms and the extent of the pathologic changes is not well demonstrated.

6. Pulmonary tuberculosis of the ordinary chronic type is demonstrated on the roentgenogram in from ten to twenty weeks after the first exposure to the disease. In almost all cases of parenchymal tuberculosis of the chronic type the roentgen findings precede the symptoms.

7. Miliary tuberculosis gives symptomatic evidence of its presence before the roentgen findings are apparent and symptoms may be present for as long as seven weeks without any roentgen evidence whatever.

8. Nodular lesions such as metastases are demonstrable when their size is 3 millimeters or more in diameter. Miliary metastases may not be seen until they are very numerous or large in size.

9. Bronchogenic carcinoma almost invariably gives positive roentgen signs, if thorough examination is done, when symptoms are present. In many cases of bronchogenic carcinoma, the roentgen findings will be present before the onset of any respiratory symptoms. Examination during expiration as well as inspiration will facilitate the early diagnosis.

Further studies of similar nature should be undertaken to determine the limitations of roentgen examination in the diagnosis of all disease processes.

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THE ROENTGEN FINDINGS IN INTRACRANIAL MASS LESIONS

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THE roentgen diagnosis and localization of intracranial mass lesions has been greatly aided by the introduction of air and other contrast media studies. From conventional film studies alone, many roentgenologists concede that a localizing diagnosis can be made in only 10 to 20 per cent of all cases. In view of this rather disappointing percentage, it was decided to critically review a consecutive series of 123 cases with proved intracranial mass lesions. Cases without adequate roentgenographic studies were omitted.

The roentgenograms of each case were studied simultaneously by both writers. There was no previous knowledge of the operative and pathologic findings, and the roentgen abnormalities were tabulated before the former were reviewed. In this way, it was unlikely that findings would be read into the roentgenograms.

Below is a specimen of the tabulation method employed for each case. For reasons of space economy, tabulation of the entire series has been omitted from this report.

Case	Age	Conventional Film Findings	Conventional Film Diagnosis	Air and Special Studies	Final Roentgen Diagnosis	Operative and Pathologic Findings
29	64m	Erosion of superior and posterior portions of the right petrous pyramid. Pineal calcified and shifted 10 mm. to the left. Normal acoustic meati (Stenvers)	Right cerebellopontine angle tumor	None	Right cerebellopontine angle	Large tumor arising from 8th nerve at cerebellopontine angle on the right. Histopathology perineurial fibroblastoma

Routine views of the skull consisted of a posteroanterior, an occipital view, and stereoscopic projections of both lateral positions. Where indicated, oblique views of the mastoids and petrous pyramids (Stenvers) and optic foramina views were obtained.

STATISTICAL FINDINGS

Table 1 indicates the histopathologic distribution of the lesions in this series. The incidence percentage does not deviate significantly from many published series.[1,2] Gliomas comprised 33.3 per cent and meningiomas 20.3 per cent of all lesions. Pituitary tumors were considerably less frequent (4.9 per cent) than in other reports, because eosinophilic adenomas were given roentgen therapy without surgery, and hence do not appear in our series.

About 50 per cent of the lesions were in individuals past forty years, with 44 per cent in patients between forty and sixty years (Table 1). The average age incidence of some of the more common lesions was:

Metastatic cancer	50 years
Meningioma	46 years
Glioblastoma multiforme	43 years
Craniopharyngioma	29 years
Astrocytoma	25 years
Medulloblastoma	6 years

In Table 11 is given the anatomic distribution of the lesions and also the age incidence. About 50 per cent were in the cerebral hemispheres, and these were mostly in patients between the ages of

TABLE I

Histopathologic Type	Age Incidence (years)								Total	Per cent
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80		
Glioblastoma multiforme	1	—	4	2	4	5	—	2	18	14.6
Astrocytoma	2	5	3	1	3	1	—	—	15	12.2
Ependymoma	1	—	—	2	—	—	—	—	3	2.4
Astroblastoma	—	—	—	—	1	1	—	—	2	1.6
Medulloblastoma	2	—	—	—	—	—	—	—	2	1.6
Oligodendroglioma	—	—	1	—	—	—	—	—	1	0.8
TOTAL GLIOMAS									(41)	(33.3)
Meningioma	—	3	—	6	8	8	—	—	25	20.3
Perineural fibroblastoma	—	—	2	2	3	1	1	—	9	7.3
Aneurysm, circle of Willis	—	1	1	1	1	1	2	—	7	5.7
Aneurysm, arteriovenous	—	—	—	1	—	—	—	—	1	0.8
Chromophobe adenoma	—	—	1	—	2	3	—	—	6	4.9
Metastatic malignancy	—	—	—	—	3	3	—	—	6	4.9
Abscess	1	3	—	—	—	—	—	—	4	3.2
Craniopharyngioma	1	—	2	—	—	1	—	—	4	3.2
Dermoid and epidermoid cyst	2	—	3	—	—	—	—	—	5	4.0
Colloid cyst	—	1	—	—	1	1	—	—	3	2.4
Subdural hematoma	—	1	—	1	—	1	—	—	3	2.4
Hemangioma	—	—	—	2	1	—	—	1	4	3.2
Chordoma	—	—	—	—	—	1	—	—	1	0.8
Hemangioblastoma	—	1	—	—	—	—	—	—	1	0.8
Retinoblastoma	1	—	—	—	—	—	—	—	1	0.8
No histopathology	—	1	—	—	—	1	—	—	2	1.6
TOTAL	11	16	17	18	27	28	3	3	123	
PERCENTAGE	8.9	13.0	13.8	14.6	21.9	22.7	2.4	2.4		

TABLE II

Location of Lesion	Age Distribution								Total
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	
Cerebral hemispheres	3	8	7	9	15	17	—	3	62
Deep toward midline					2	2			4
Supratentorial midline	1	2	4	2	2	4	—	—	15
Cerebellar	5	5	—	2	—	—	—	—	12
Other infratentorial	—	—	—	1	1	—	—	—	2
Pituitary	—	—	1	—	2	3	—	—	6
Orbit	3	—	1	—	—	—	—	—	4
Aneurysms at base	—	1	1	2	1	1	2	—	8
Cerebellopontine angle	—	—	2	2	3	1	1	—	9
Arising from paranasal sinuses	—	—	1	—	—	—	—	—	1

forty and sixty years. Infratentorial lesions made up 18.7 per cent, occurring mainly in individuals below the age of twenty.

The high percentage of cases where localization could be made on conventional film studies came as a considerable surprise to us. Table III illustrates the diagnostic efficacy of conventional film studies and also of additional air studies. From roentgenograms made without contrast media,

a localizing diagnosis was made in about 50 per cent of all cases. A high percentage of localization is not surprising in pituitary tumors or in dermoid and epidermoid cysts because of their characteristic destructive effect on the bony structures. Of the 9 cerebellopontine angle lesions, diagnosis was made in 8. This high percentage is largely due to the changes seen on oblique views of the pyramids, where enlargement of the porus acusticus can be seen. Of the 25 meningiomas, 16 were localized on the routine films. Of these only 8 showed tumor calcification or bone sclerosis. Dyke[4] found that about 50 per cent of meningiomas produced localizing changes on the roentgenogram. Infratentorial lesions generally could not be accurately localized on conventional roentgenograms. Commonly there was indirect evidence of increased intracranial pressure.

A word about localization. While usually the localization could be made with considerable accuracy, in cases where only a pineal shift was found, obviously we could indicate the side of the lesion, but no more. This was deemed sufficient to include with other cases localized by conventional films.

Lesions were suspected in 18 (14.5 per cent) cases. The roentgen findings in this group consisted mainly of evidence of increased intracranial pressure, widened sutures, increased convolutonal markings, and erosion or marked demineralization of the dorsum sellae.

In only 44 patients (35.8 per cent) were the conventional films completely negative. Thus, there were either definite localizing findings or suspicion of an expanding intracranial lesion in 64.1 per cent of all the conventional roentgen examinations.

Air studies were done on 50 patients. Of

TABLE III

Histopathologic Type	Total	Conventional Films. Conclusions			Air Studies Done	Localization Made from Air Studies Where Conventional Films Failed to Localize
		Localization Made	Tumor Suspected	Negative		
Meningioma	25	15	3	7	13	6
Glioblastoma multiforme	18	7	4	7	11	7
Astrocytoma	15	5	5	5	8	5
Other gliomas	8	1	4	3	1	1
Pituitary tumors	6	6	—	—	—	—
Perineural fibroblastoma	9	8	—	1	—	—
Aneurysm	8	4	—	4	4	2*
Craniopharyngioma	4	3	—	1	—	—
Colloid cyst	3	—	1	2	3	3
Metastatic carcinoma	6	2	—	4	4	3
Abscess	4	—	1	3	1	1
Dermoid and epidermoid cyst	5	4	—	1	—	—
Subdural hematoma	3	2	—	1	2	1
Hemangioma	4	2	—	2	2	1
Chordoma	1	1	—	—	—	—
Hemangioblastoma	1	—	—	1	—	—
Retinoblastoma	1	—	—	1	—	—
No histopathology	2	1	—	1	1	—
	123	61 49.6%	18 14.5%	44 35.8%	50 40.7%	30 24.4%

* Cisterna chiasmatis failed to fill.

TABLE IV

Location	No. Cases	Sellar Erosions and Deformities	Demineralization of Dorsum	Widened Sutures	Increased Digital Markings	Calcification	Table Changes	Sphenoidal Fissure Changes	Petrous Pyramid Erosions	Pineal Displacement	Choroid Displacement	Orbital Bone Changes	Enlarged Internal Auditory Meatus	Displaced Falx	Increased Table Vascularity
Frontal and frontoparietal	37	1	6	1	1	4	7	—	—	8	—	2	—	—	1 Depressed Cribriform Plate 1
Posterior parietal and occipital	7	2	1	—	1	2	1	1	—	1	1	—	—	—	—
Temporal	13	—	2	1	1	3	1	3	1	2	1	—	—	1	—
Intrasellar	6	6	—	—	—	—	—	1	—	—	—	—	—	—	—
Suprasellar and parasellar	21	6	—	1	—	4	—	4	1	3	—	2	—	—	—
Deep-seated near midline	3	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Midline and ventricular	12	3	1	4	3	1	—	—	—	—	—	—	—	—	—
Orbital	4	—	—	—	—	—	—	1	—	—	—	3	—	—	—
Cerebellar	10	—	3	7	7	—	—	—	—	—	—	—	—	—	—
Cerebellopontine	10	1	1	—	—	1	—	—	3	3	—	—	6	—	—
TOTAL	123	19	15	14	13	15	9	10	5	17	2	7	6	1	1
PERCENTAGE		15.5	12.2	11.4	10.6	12.2	7.3	8.1	4.05	13.8	1.6	5.7	4.8	0.8	0.8

TABLE V

Histopathology	No. Cases	Sellar Changes	Calcification	Suture Widening	Pyramid Changes	Sphenoidal Fissure Changes	Increased Table Vascularity	Table Changes	Pineal Displacement	Localized Hyperostosis
Meningioma	25	7	3	—	2	4	—	5	5	5
Glioblastoma multiforme	18	6	—	2	—	1	—	—	5	—
Astrocytoma	15	4	4	5	—	1	—	—	—	—
Other gliomas	8	2	1	2	—	—	—	1	—	—
Pituitary tumors	6	6	—	—	—	1	—	—	—	—
Perineural fibroblastoma	9	2	1	—	7	—	—	—	2	—
Aneurysms	8	1	2	—	—	1	—	—	—	—
Craniopharyngioma	4	2	3	1	—	—	—	—	—	—
Colloid cyst	3	1	—	—	—	—	—	—	—	—
Metastatic carcinoma	6	—	—	—	—	—	—	—	2	—
Abscess	4	—	—	2	—	—	—	—	—	—
Dermoid and epidermoid	5	—	—	—	—	1	—	1	—	—
Subdural hematoma	3	—	—	—	—	—	—	1	2	—
Hemangioma	4	2	—	—	—	—	1	1	—	—
Chordoma	1	1	1	—	—	1	—	—	1	—
Hemangioblastoma	1	—	—	1	—	—	—	—	—	—
Retinoblastoma	1	—	—	—	—	—	—	—	—	—
No histopathology	2	—	—	1	—	—	—	—	—	—
TOTAL	123	34	15	14	9	10	1	9	17	5
PERCENTAGE		27.7	12.2	11.4	7.3	8.1	0.8	7.3	13.8	4.1

these, only 2 were negative in the presence of a proved tumor. One was a meningioma in the occipital region near the midline. With air studies, localizing diagnosis was made in 30 cases where the conventional film findings were negative or indeterminate. A total of 74.0 per cent of all the intracranial lesions were thus localized by routine film studies and/or air studies. Many patients, however, in spite of negative findings on the routine film studies, did not have air studies because of clearcut clinical localizing symptoms. This was particularly true of children with cerebellar lesions.

Tables IV and V are statistical compilations of the abnormal roentgen findings in all the cases of this series. The roentgen findings are correlated with the location of the lesion (Table IV) and with the histopathologic diagnosis (Table V).

Sella Turcica. Changes in the sella turcica were the most common abnormal roentgen finding in the series, occurring in 34 cases (27.6 per cent). Characteristic sellar changes were found in practically all the pituitary tumors, i.e., ballooning of the sella, erosion or thinning of the posterior clinoids and dorsum, and sharpening of the anterior clinoids. In one case, however, the dorsum was destroyed, but the rest of the sella was intact. This could not be distinguished roentgenologically from increased intracranial pressure with erosion of the dorsum (Fig. 2). In suprasellar and parasellar lesions, pressure erosions of the dorsum or floor of the sella were seen in 6 of the 21 cases. In extrasellar tumors, where no direct pressure could be exerted against this structure, the changes in the dorsum are usually the result of the increased intra-

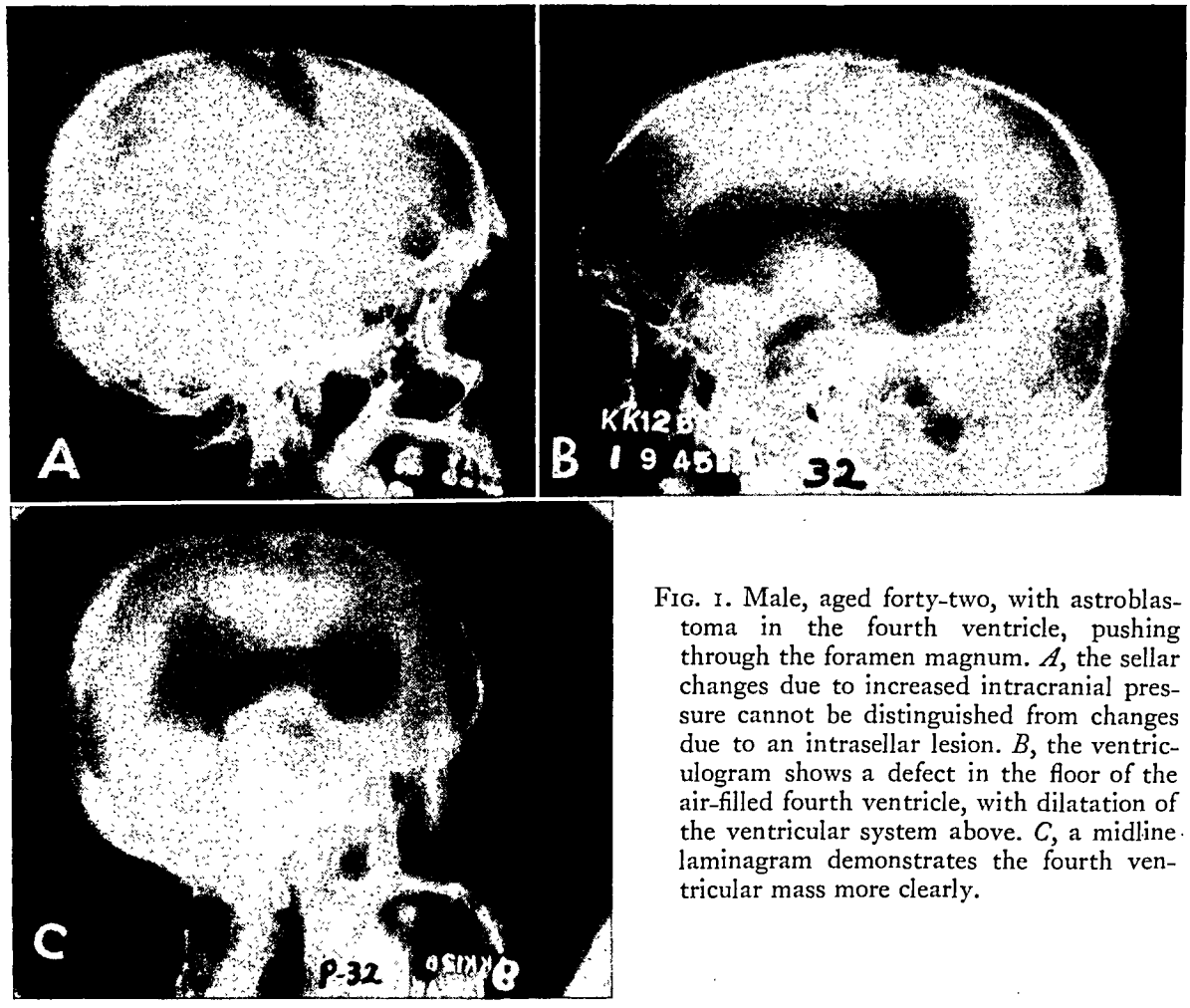


FIG. 1. Male, aged forty-two, with astroblastoma in the fourth ventricle, pushing through the foramen magnum. *A*, the sellar changes due to increased intracranial pressure cannot be distinguished from changes due to an intrasellar lesion. *B*, the ventriculogram shows a defect in the floor of the air-filled fourth ventricle, with dilatation of the ventricular system above. *C*, a midline laminagram demonstrates the fourth ventricular mass more clearly.

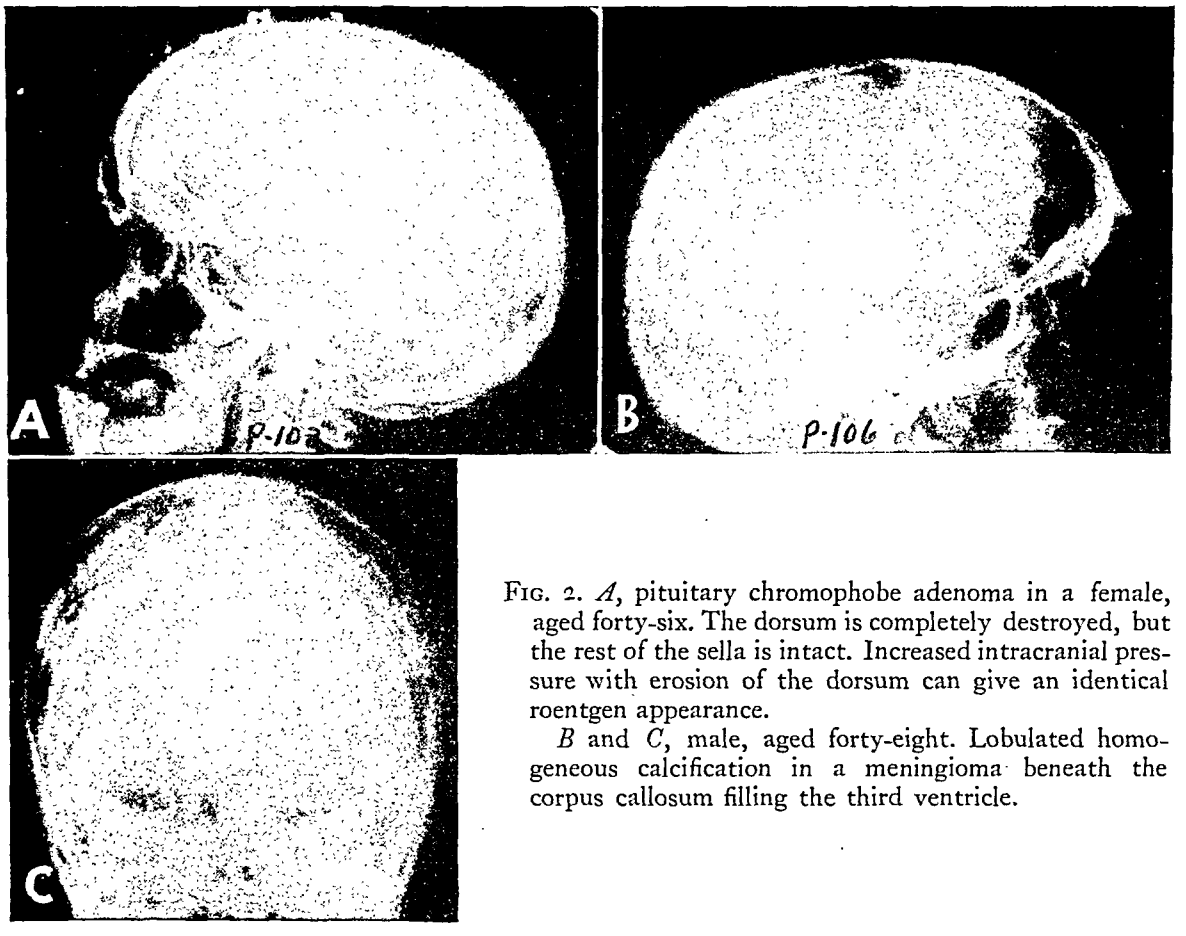


Fig. 2. *A*, pituitary chromophobe adenoma in a female, aged forty-six. The dorsum is completely destroyed, but the rest of the sella is intact. Increased intracranial pressure with erosion of the dorsum can give an identical roentgen appearance.

B and *C*, male, aged forty-eight. Lobulated homogeneous calcification in a meningioma beneath the corpus callosum filling the third ventricle.

cranial pressure where the dilated third ventricle was pulsating against the dorsum. However, this may closely simulate a suprasellar or even an intrasellar lesion (Fig. 1). It may be extremely difficult if not impossible to distinguish dorsum erosion from demineralization. Of the 34 cases with sellar changes, we considered 15 to be demineralization only.

Calcifications. In 16.3 per cent of the

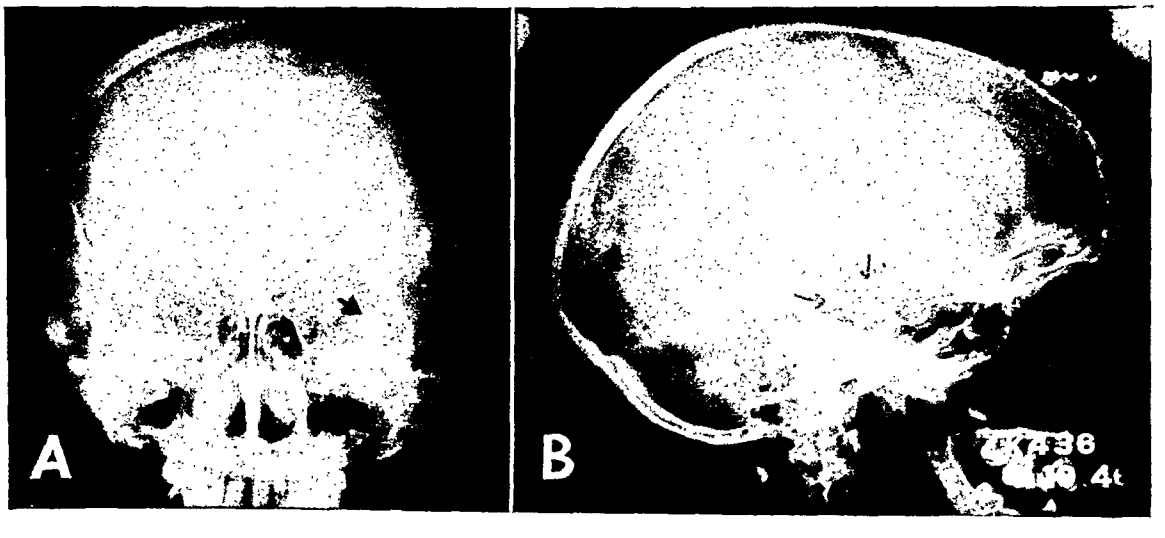


Fig. 3, *A* and *B*. Female, aged eleven. Astrocytoma of the left temporal lobe with amorphous calcification.

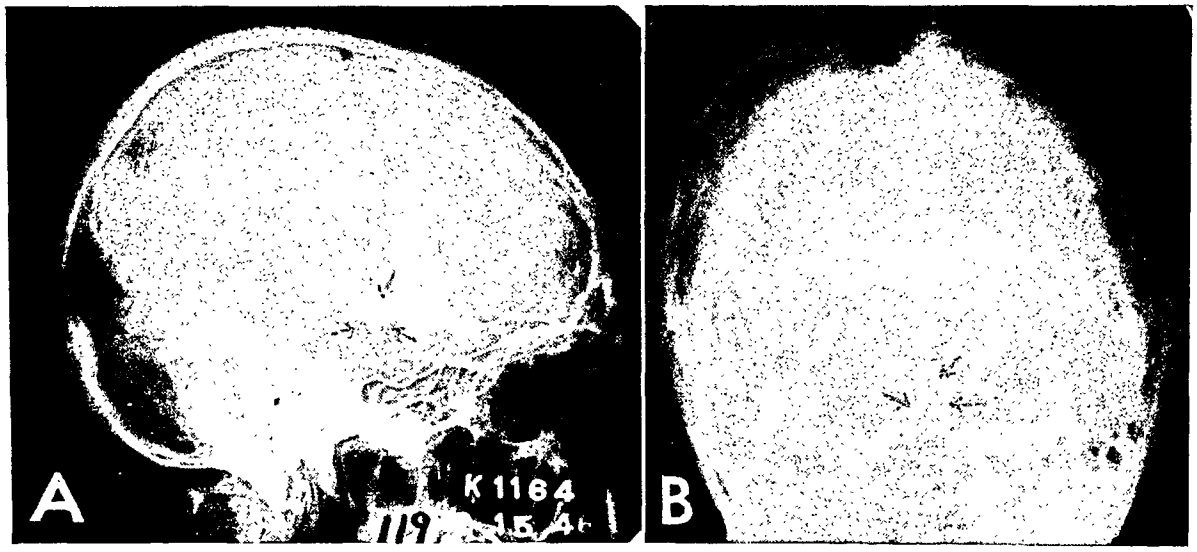


FIG. 4, *A* and *B*. Male, aged twenty-eight. Irregular calcification above the sella in a craniopharyngioma.

cases there was calcification within the lesion or a sclerotic bone reaction in the immediate vicinity (Table v). These changes were seen in about one-third of the meningiomas (Fig. 2*A*). In these latter tumors, localized hyperostosis occurred more often than amorphous calcification. Characteristic spicule formation in the tables was seen only once in the 25 cases of meningioma. About one-fourth of the astrocytomas showed calcification, usually of the fine granular variety (Fig. 3). Of the 4 craniopharyngiomas, 2 showed the characteristic calcification in the midline above the sella (Fig. 4). Thin crescentic calcification appeared in 2 of the 8 aneurysms (Fig. 5). The single oligodendroglioma of the series was heavily calcified (Fig. 6). Not one of the 18 glioblastomas was calcified, and only one of the less common gliomas showed calcium deposits.

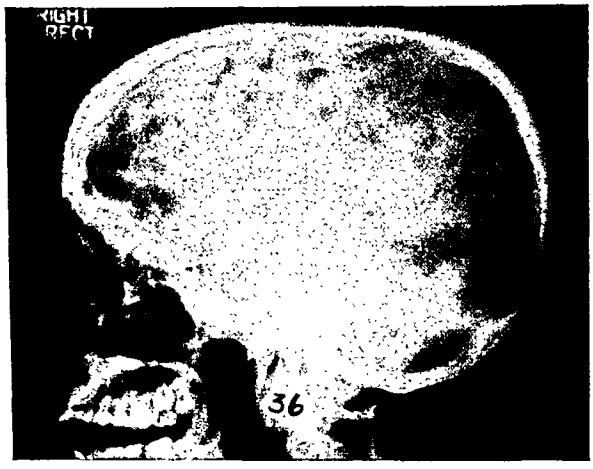


FIG. 5. Male, aged eighteen. The thin crescentic calcification in the right occipitoparietal area near the midline was within the wall of a large arteriovenous aneurysm between the posterior cerebellar artery and the vein of Galen. Note the roentgen evidence of increased intracranial pressure.

Suture Separation and Increased Digital Markings. Widening of the sutures was observed in 14 cases. Half of these were in cerebellar lesions, and 5 others in midline or intraventricular lesions, with internal block hydrocephalus (Fig. 7 and 14). In only 2 cases were widened sutures observed in hemispheric lesions. The average age for suture separation was ten years. In older individuals with firmer sutures, long-standing internal hydrocephalus and increased intracranial pressure was more apt to produce exaggerated convolutional markings and demineralization of the dorsum sellae.

Increased convolutional markings were observed in 13 cases. It is extremely difficult if not impossible to consider the markings definitely exaggerated unless these findings are quite advanced. There is too great a variation in convolutional markings

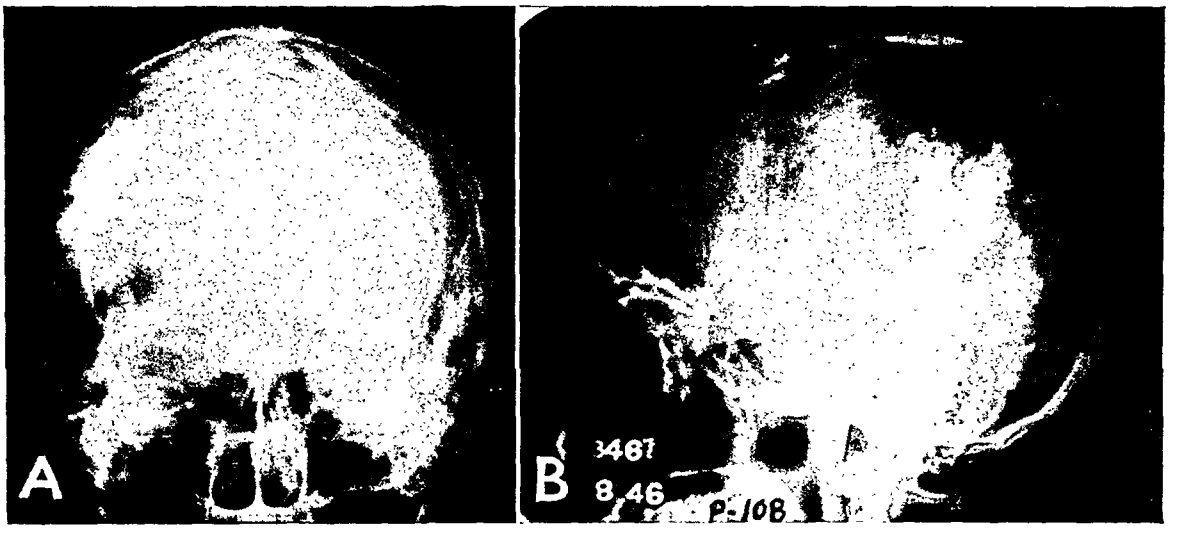


Fig. 6, *A* and *B*. Male, aged twenty-eight. Oligodendroglioma arising from the right temporal lobe with extensive amorphous calcification in the tumor.

in normal skulls, and technical factors which change film contrast make decided variations in these markings even in the same skull. Over half the cases with definitely increased markings had cerebellar lesions.

Petrous Pyramid Changes. Abnormalities of the petrous pyramids from pressure erosion or invasion were seen in 9 cases (7.3 per cent), Of special interest are the findings in 9 cases of perineural fibroblastoma of the eighth nerve. In 3 cases, definite erosion of the superior and posterior margins of the pyramid was apparent. In 4 cases, without definite pyramid erosion, roentgenograms taken in Stenvers' position showed one internal acoustic meatus definitely enlarged (Fig. 8 and 9). This was not apparent on posteroanterior or occipital views. As a control, 35 patients without cerebellopontine angle signs or symptoms were studied with Stenvers views of the pyramids. In almost all these cases, the internal auditory meati were clearly seen, and there was no significant difference in size of the left and right meati. This com-



Fig. 7, *A* and *B*. Male, aged fourteen. Widened sutures and increased digital markings from increased intracranial pressure. Hemangioblastoma of the left cerebellar hemisphere.

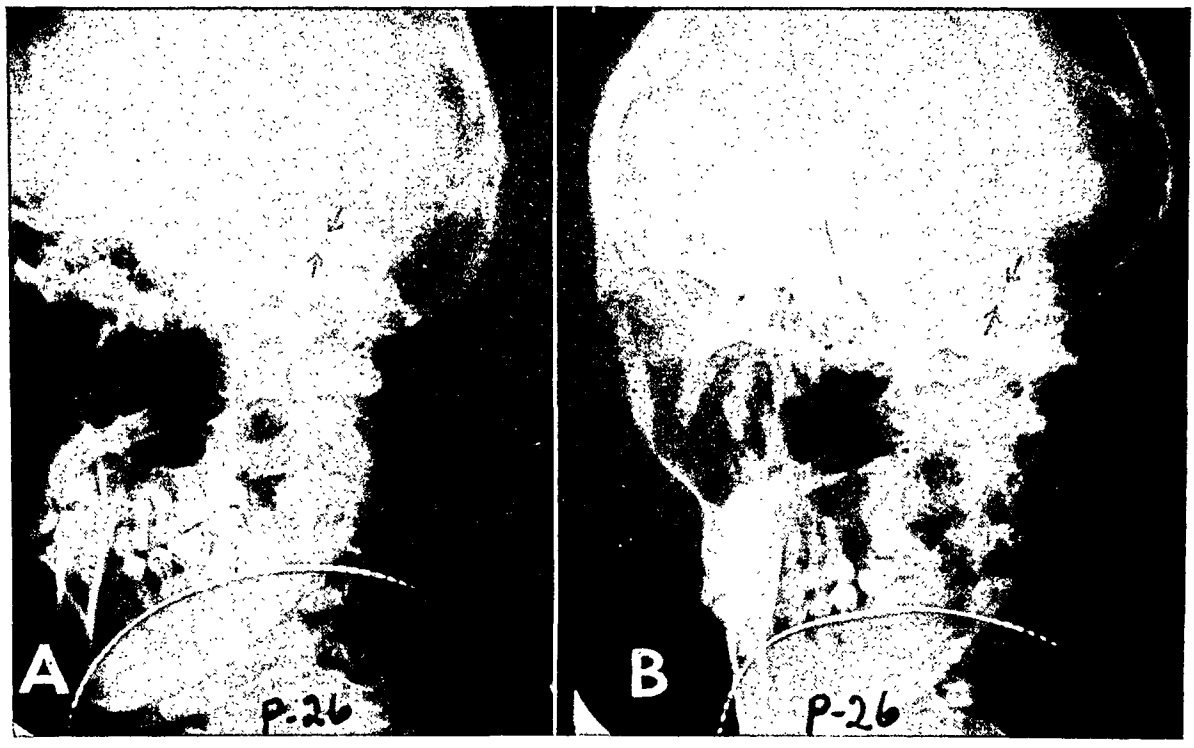


FIG. 8, *A* and *B*. Female, aged twenty-five. Stenvers views of the pyramids showing widened left porus acusticus from perineural fibroblastoma arising from the left eighth nerve. *B* is the left side.

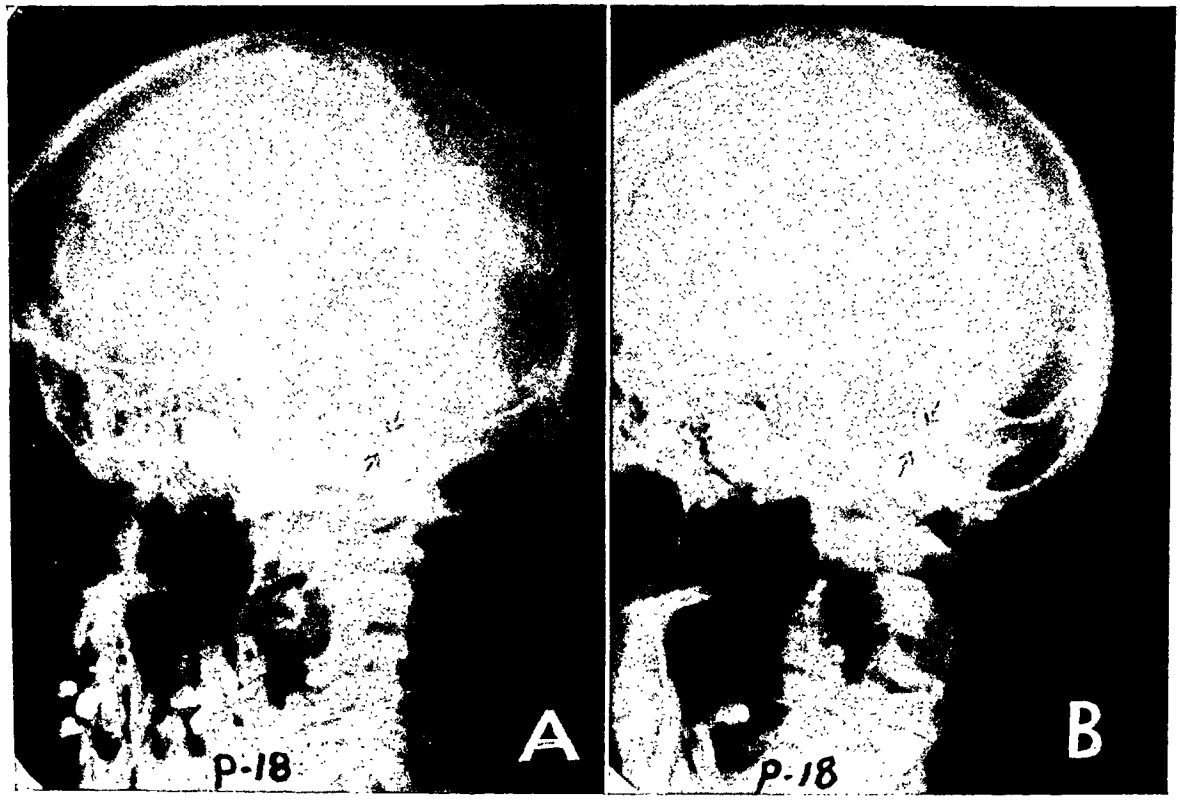


FIG. 9, *A* and *B*. Female, aged thirty-eight. Perineural fibroblastoma arising from the left eighth nerve. *B* shows the widened left porus acusticus compared to the right (*A*).

plete symmetry of normal internal auditory meati proves that enlargement of one meatus in a patient with suspected angle lesion is of great diagnostic significance. The oblique Stenvers view therefore becomes an indispensable aid in the roentgen diagnosis of angle lesions. In one case of acoustic neuroma, there was the most unusual finding of a ring-like calcification behind the pyramid, due to calcification of the rim of the tumor (Fig. 10). In only one of these cases were the roentgen findings completely negative, but no Stenvers views were made in this patient, preoperatively.

Sphenoid Bone Changes. Changes in the sphenoid wings and fissures were found in 10 cases (0.8 per cent). Of these, 4 were from local tumor pressure. In 3 cases, temporal lobe lesions, with swelling and edema of the temporal lobe, led to pressure demineralization of the homolateral sphenoid wings. A unilateral hemispheric tumor, with increased pressure unilaterally, can also produce this unilateral demineralization of the sphenoid wings (2 cases). Meningiomas are the most common lesion directly involving the wings. Bone erosion or hyperostosis or even both may result. Asymmetry of the fissures without bony involvement cannot be considered of diagnostic significance.



Fig. 10. Male, aged fifty-five. Perineural fibroblastoma just behind the right internal auditory meatus. The ring-like calcification within the tumor is most unusual in this type of lesion.

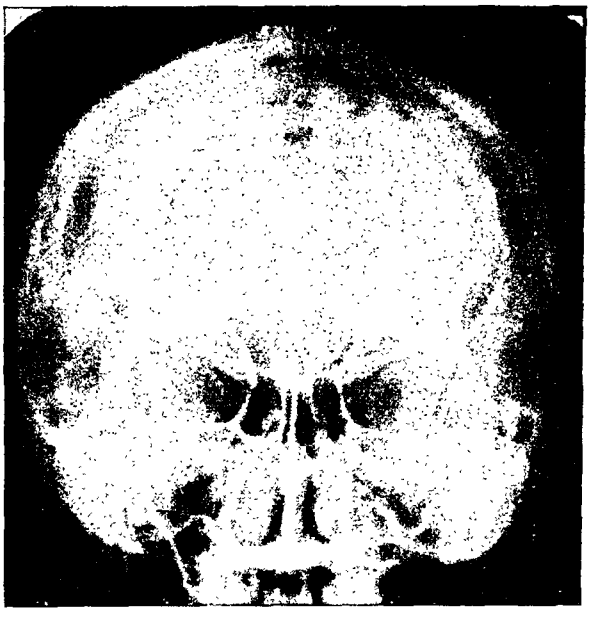


Fig. 11. Female, aged thirty-four. The numerous wide vascular channels in the frontal bone at the vault were due to a meningeal hemangioma attached to the left side of the longitudinal sinus.

Erosions of the Tables. Erosions of the tables of the skull indicate a mass against or within the bone. Of the 9 cases with erosion of the tables, 5 were meningiomas. An epidermoid and hemangioma accounted for 2 others.

Enlargement of the vascular channels in the calvarium proved to be an uncommon and inaccurate roentgen sign of an intracranial lesion. There is too great a normal variation in size and number of vascular channels, often with unilateral preponderance. However, in one of our cases (Fig. 11), there was a collection of very large channels due to a meningeal hemangioma. While not to be overlooked, unusual vascular channels do not constitute a dependable localizing roentgen sign.

Lateral Pineal Shifts. A lateral shift of the calcified pineal body, in our opinion, is one

of the most important findings to be searched for in cases of suspected intracranial mass lesions. We feel its importance has not been sufficiently emphasized in the past.

In our series, the pineal body was calcified in 27.6 per cent. The average age of patients with calcified pineal was 48.3 years, with the youngest in a girl aged thirteen. Pineal calcification is known to increase in the older age groups.

Of the 35 cases with a calcified pineal, in 17 there was a significant lateral displacement. Table VI gives full information of the degree of shift and location of the underlying lesion.

TABLE VI

PINEAL DATA

Pineal Calcifications—35
Lateral Shift —17
Backward Shift — 1 (sphenoid meningioma)

	Location of Lesion	Pineal Lateral Shift	Pineal Seen No Shift
	Cerebellopontine	3	2
	Hemisphere (cerebral)	10	3
	Middle fossa	2	2
	Subdural hematoma	2	—
	Carotid aneurysm	—	2
	Suprasellar	—	3
	Intrasellar	—	3
	Orbital	—	1
	Cerebellar	—	1
	TOTAL	17	17

Millimeters of Lateral Shift (Difference between the 2 measurements to right and left outer tables): 15, 13, 13, 13, 10, 10, 10, 10, 9, 9, 9, 5, 5, 5, 4, 4, 4,

Average shift = 8.8 mm.

Cases where shifted pineal only roentgen finding 11

The technique of measuring for pineal shift is extremely simple. Measurement is made from the midportion of the calcification directly lateral to the outer table of each side. A difference of 4 mm. or more between the two measurements is considered significant of pineal displacement. While it is important for the head to be well centered on the anteroposterior view (pineal best seen on the anteroposterior rather than on the posteroanterior view), rotation up to 10 or 15° does not significantly alter the measurements. We measured many normal cases in poorly centered anteroposterior views, but found no measurement difference greater than 3 mm. unless there was over 15° rotation. In our series there were shifts as great as 15 mm., with an average of 8.8 mm.

A word about identification of the calcified pineal body. Not rarely, the pineal is seen on the lateral view, but on anteroposterior projection it cannot be identified, or it may be confused with a portion of calcified falx, or bony condensation in the occipital bone. In this situation, a stereoscopic pair in the anteroposterior projection will make certain identification of the pineal possible.

Table VI indicates that cerebral hemispheric tumors are most apt to produce lateral pineal shifts. Of the 17 displaced pineals, 10 were from hemispheric tumors, and 2 from subdural hematomas over the hemispheres. In only 3 cases were calcified pineals not displaced by hemispheric mass lesions. Lesions around the midline, base, or beneath the tentorium rarely lead to lateral pineal shift. In 11 cases, the pineal displacement was the *only* roentgen finding, while in 6 cases there were other localizing roentgen findings. It is interesting that 3 of the 10 cases with angle tumors showed lateral pineal shift.

Most investigators have shown more interest in sagittal displacements of the pineal, for which many ingenious measuring devices and methods have been presented.[3,5,7] From our experience, lateral shifts are not only more common but easier

to determine accurately, even when slight. Although a number of cases with lateral shift also showed pineal shift in the sagittal plane, in only one instance was there a definite backward displacement without lateral deviation. This was in a patient with a basisphenoid meningioma.

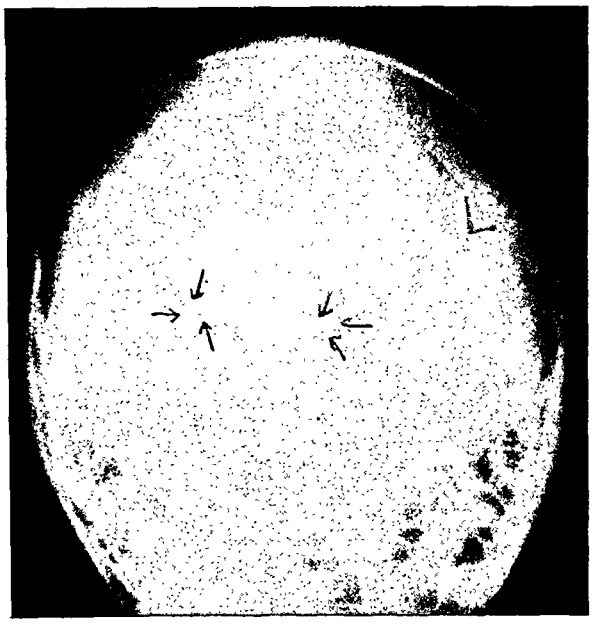


Fig. 12. Male, aged fifty-two. The calcified choroid plexus on the left is displaced considerably to the right by metastatic carcinoma invading the left parietal lobe.

It must be borne in mind that a displacement of the pineal to one side means a probable mass lesion on the other side only when tumor or mass is suspected. Cerebral atrophy, scarring or agenesis will usually pull the pineal toward the affected side.

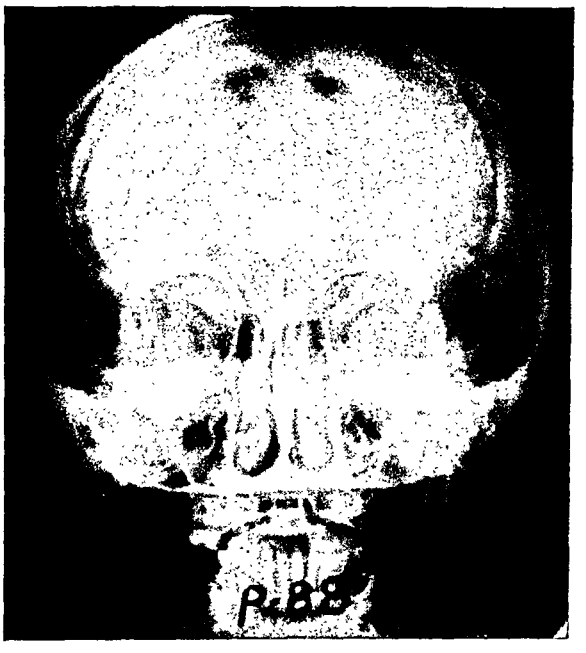


Fig. 13. Female, aged forty-three. Meningioma of the frontal lobes. This tumor was adherent to the cribriform plate. Note the irregular, uneven cribriform plate.

Displacement of the calcified choroid plexus is a rather unusual finding[4,6] (Fig. 12). It was seen in 2 cases of the series, both in patients with cerebral hemispheric tumor. In one, there was also a pineal shift

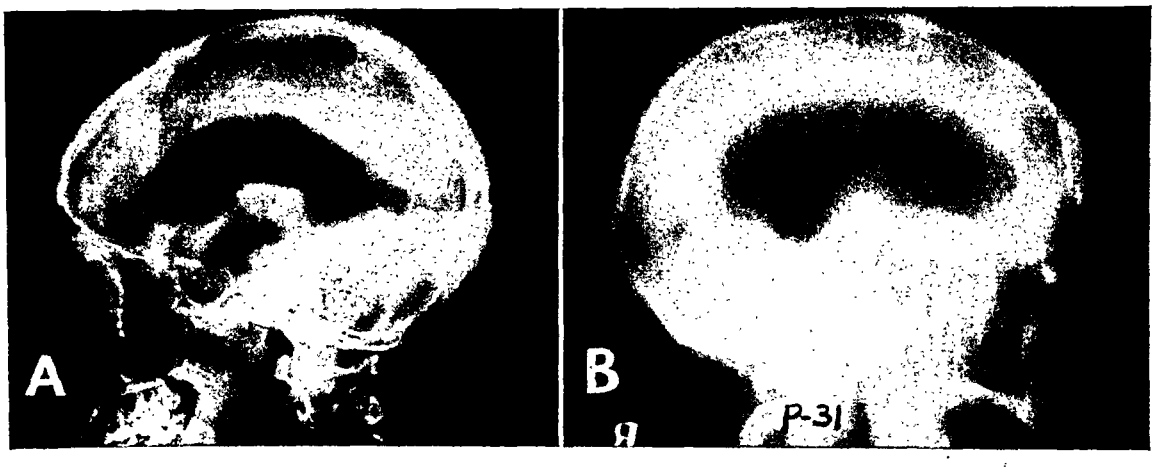


Fig. 14. Two cases of colloid cyst of the third ventricle. *A*, female, aged twenty. Defect in the posterior portion of third ventricle with dilatation of the third and lateral ventricles. *B*, male, aged fifty-eight. A midline laminagram clearly demonstrates the smooth mass in the third ventricle.

to corroborate the diagnosis, but in the other the displacement of the calcified choroid was the sole roentgen finding upon which a diagnosis could be made.

A displacement of the calcified falx was found in a patient with a temporal lobe tumor. This was the only clue to the roentgen diagnosis.

In a case of frontal lobe meningioma, adherent to the cribriform plate, there was a detectable deformity of the plate on the posteroanterior view (Fig. 13).

SUMMARY

1. Roentgen, pathologic and anatomic correlations were made in 123 proved cases of intracranial mass lesions.

2. With routine conventional film studies alone, 49.6 per cent of these cases were localized. With routine roentgenograms and air studies, 74.4 per cent localization was obtained. Only 35.8 per cent of the cases were completely negative on routine skull roentgenograms.

3. Changes in the sella turcica occurred in 27.6 per cent. Intrasellar and extrasellar lesions usually gave characteristically different roentgen changes in the sellar area.

4. Tumor calcification was seen in 12.2 per cent. Meningiomas, astrocytomas, craniopharyngiomas and aneurysms calcified more often than other lesions. Bone sclerosis occurred in 4.0 per cent, from meningioma in all cases.

5. In 11.4 per cent there were widened sutures. This was most common in children with cerebellar lesions.

6. Petrous pyramid erosion and/or widening of the internal auditory meatus were found in 7 of 9 patients with acoustic perineural fibroblastoma. Stenvers views are important for detection of meatal enlargement.

7. Sphenoidal fissure or wing changes were seen in 8.1 per cent. A swollen temporal lobe from local lesion or from generalized increased intracranial pressure may cause demineralization of the sphenoidal wings.

8. The pineal was calcified in 27.6 per cent. About 50 per cent of these showed a significant lateral displacement. Most mass lesions in the hemispheres will displace the pineal to the opposite side. More attention seems warranted to the lateral shift of the pineal than to displacement in the sagittal plane.

We wish to express our sincere gratitude and thanks to Dr. Paul C. Swenson, Professor of Radiology, and to Dr. Rudolph Jaeger, Professor of Neurosurgery, for their cooperation and kindness in making the clinical and roentgen material available to us.

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VOL. 61, No. 6

COMPLETE BLOCK OF THE LUMBAR SPINAL CANAL DUE TO HERNIATION OF THE NUCLEUS PULPOSUS*

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COMPLETE obstruction of the spinal canal by protrusion of the nucleus pulposus of the lumbar intervertebral discs is infrequent. The cases reported up to the present time have been associated with severe symptoms referable to compression of the cauda equina, and in many the differential diagnosis between tumor of the cauda equina and herniated disc could not be made. A review of 150 lumbar myelograms done during the past five years disclosed 5 patients with complete spinal canal block. Four of these had little to suggest compression of the cauda equina, while in the fifth the clinical diagnosis was a cauda equina tumor.

The purpose of this report is to show that complete lower spinal canal block may occur without the signs of cauda equina compression. This can be diagnosed only with pantopaque myelography. In addition, a variation in myelographic technique to outline the superior and inferior margins of the obstructive lesion is described.

CASE REPORTS

CASE 1. M. R. (Hosp. No. 292293), male, aged fifty-nine, first complained of low back pain twenty-one months before admission following mild exercise. This persisted for a few days and then radiated down the posterior aspect of his left leg. It disappeared and recurred intermittently with varying intensity on several occasions apparently without cause. When the pain was most intense he was completely incapacitated. On several occasions he noted numbness in his left foot and the outer aspect of his right thigh. Some aggravation of pain occurred on straining. He did not respond to conservative orthopedic treatment.

Examination showed that his left calf was atrophied 0.5 cm. The ankle jerks were absent bilaterally. Sensory responses and motor power were normal.

Plain roentgenographic examination of the lumbosacral spine on several occasions showed osteoarthritic changes in the lower lumbar vertebrae and narrowing of the lumbosacral interspace.

Myelography after the instillation of 3 cc. of pantopaque between the third and fourth lumbar vertebrae showed an abrupt transverse block about 1 cm. above the inferior margin of the fourth lumbar vertebra when the patient was in the erect position. Small dentate irregularities were present at the caudal end of the pantopaque column. Within the column was a radiolucent streak parallel to the long axis of

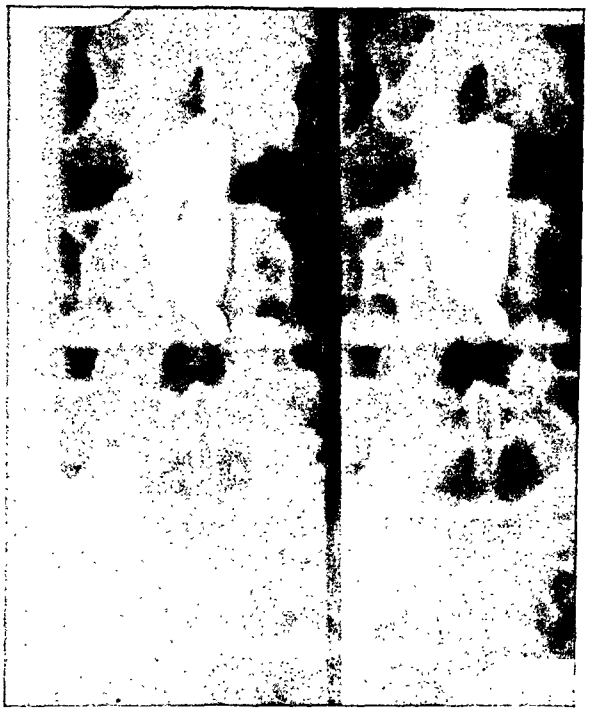


FIG. 1. Case 1. Spot roentgenogram with patient in erect position shows a transverse block above the level of the inferior margin of the fourth lumbar vertebra with dentate serrations of the distal end of the pantopaque column. In the middle of the pantopaque column is a linear radiolucent shadow which at operation was found to be due to edematous nerve roots.

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the spinal canal indicative of a swollen nerve root.

The spinal fluid proteins were 100 mg. per 100 cc.

Preoperative diagnoses ran the gamut from psychoneurosis to cauda equina tumor.

A laminectomy of the fourth and fifth lumbar vertebrae was performed and extradural exploration did not disclose the cause of the block. Intradural exploration at first failed to reveal a mass, but the roots of the cauda equina were markedly swollen. Finally the protruded disc was divulged as a bulge in the midline anteriorly and removed through a transdural incision. The disc was large, measuring more than 4 cm. in length.

The patient made an excellent recovery.



FIG. 2. Case II. Spot roentgenogram with patient in the erect position shows a somewhat oblique line of block at the distal end of the pantopaque column.

CASE II. J. B. (Hosp. No. 303464), male, aged fifty-five, complained of low back pain for more than twenty years, which was never severe enough to incapacitate him. His attacks occurred from two to three times a year and were relieved by heat. There was no history of injury. Seven months before admission he developed low back pain radiating down the posterior aspect of his right thigh and leg and aggravated by motion and strain. Four months later the pain radiated down the posterior aspect of his left leg and slight numbness along the inner side of his right foot appeared.

The patient was confortable when examined. Extension of his spine was limited and pain was aggravated by bending sideways and on hyperextension of both legs, more marked on the right side. The right cremasteric and left abdominal reflexes were diminished, and the ankle and knee jerks were absent bilaterally. There were no sensory changes.

Plain roentgenograms of the lumbosacral spine showed narrowing of the lowermost three intervertebral spaces and moderate osteoarthritic changes involving the lower lumbar spine.

Lumbar puncture between the fifth lumbar and first sacral vertebrae was dry. A second tap between the second and third lumbar vertebrae was successful, and manometric determinations at this site were normal. Myelography after the instillation of 3 cc. of pantopaque revealed a complete block at the level of the inferior margin of the fourth lumbar vertebra. The distal end of the column was irregular but not broadened, and a small concave indentation was present. Several radiolucent streaks parallel to the long axis of the cord indicative of swollen nerve roots were present. A shallow indentation in the left side to the pantopaque column at the interspace between the second and third lumbar vertebrae was seen, interpreted as due to a degenerative disc change.

The spinal fluid proteins were 175 mg. per 100 cc., and the globulin content was three plus.

The roentgen diagnosis was obstruction due to central protrusion of a herniated disc. In view of the high proteins the clinical diagnosis favored cauda equina tumor.

A laminectomy of the fourth and fifth lumbar vertebrae was performed. The lesion could not be seen extradurally. When the dura was incised and the cauda equina drawn aside the protruded disc was readily brought into view. The visible protrusion measured 2 by 2 cm. and angulated the cauda equina posteriorly. The disc was removed through a transdural incision, and the patient made an excellent recovery.

CASE III. C. K. (Hosp. No. 306573), a male, aged twenty-nine, first complained of low back pain immediately after holding a heavy weight two years ago. He had been flexed for about five minutes and then was unable to straighten his

back. This gradually abated and he was free from pain for about two weeks. The low back pain then recurred and was worse in the morning, but improved as the day went on. Periods of remission and exacerbation were frequent, the painful episodes lasting about two weeks. For six months before admission he had more or less constant pain radiating down the posterior and lateral aspects of both thighs and legs as far as the lateral malleoli, and scattered areas of paresthesia were present. The pain was aggravated by straining.

Examination showed a loss of the usual lumbar lordotic curve and pronounced spasm of the erector spinae muscles. There was limitation of flexion and extension with reference of pain to the lateral aspects of both thighs. A bilateral Lasègue's sign was present. The reflexes were normal, and hypesthesia of the right leg up to the thigh was found.

Plain roentgenograms showed straightening of the usual lumbar lordotic curve and narrowing of the lumbosacral interspace.

Myelography after the injection of 3 cc. of pantopaque between the third and fourth lumbar vertebrae showed a complete transverse block at the level of the middle of the fourth lumbar vertebra with dentate serrations in the caudal end of the pantopaque column. Several negative shadows parallel to the long axis of the spinal canal were considered indicative of swollen nerve roots.

About 2 cc. of the pantopaque was removed, and the interspace between the fifth lumbar and first sacral vertebrae was tapped. After the injection of 2 cc. of pantopaque the patient complained of severe pain, no doubt due to distention of the caudal sac. With the patient turned into the head-down position the inferior margin of the blocking lesion was identified at the level of the interspace between the fourth and fifth lumbar vertebrae as a transverse block with two small vertical projections of pantopaque passing between swollen nerve roots. No defects at the lumbosacral interspace were seen. The findings were interpreted as complete block due to a central protrusion of a herniated intervertebral disc. Following examination the



FIG. 3. Case III. *A*, spot roentgenogram with the patient in the erect position shows a transverse block at the midportion of the body of the fourth lumbar vertebra with dentate serrations at the distal end of the column. *B*, the upper aspect of the block is shown with the patient in the erect posture. Two cubic centimeters of pantopaque have been instilled into the caudal sac. *C*, the lower margin of the block is identified with the patient in the head-down position just above the superior margin of the fourth lumbar vertebra.

oil was withdrawn without difficulty and the patient's pain vanished.

Manometric determinations above the level of the block were normal. Below the block manometrics were indicative of a complete obstruction, with an initial pressure of 50 mm. of water, no rise on jugular compression and a rapid fall to zero pressure.

The spinal fluid protein content was 29 mg. per 100 cc. above the block and 31 mg. per 100 cc. below.

Laminectomy of the fourth and fifth lumbar vertebrae was performed. Extradural exploration was negative, but on opening the dura a large midline disc protruding slightly towards the right was readily observed and removed without difficulty through a transdural incision.

The patient made an excellent recovery.

CASE IV. S. W. (Hosp. No. 305698), male, aged fifty-five, had a sudden knife-like pain in the lower back while lifting a heavy beam three months before admission. He was unable to straighten his back, and the pain was aggravated by slight strain. This disappeared after bed rest, but recurred three weeks later, accompanied by pain down the lateral aspect of the left thigh and leg. He was admitted because of the low back pain.

Examination showed a flattening of the usual lumbar lordotic curve, with limitation of flexion and extension because of pain. There was no tenderness on pressure over the spine or pelvis. Straight leg raising on the right side caused pain on the left side, and raising the left leg produced severe discomfort. No sensory changes or pathologic reflexes were noted. The left knee jerk was slightly reduced.

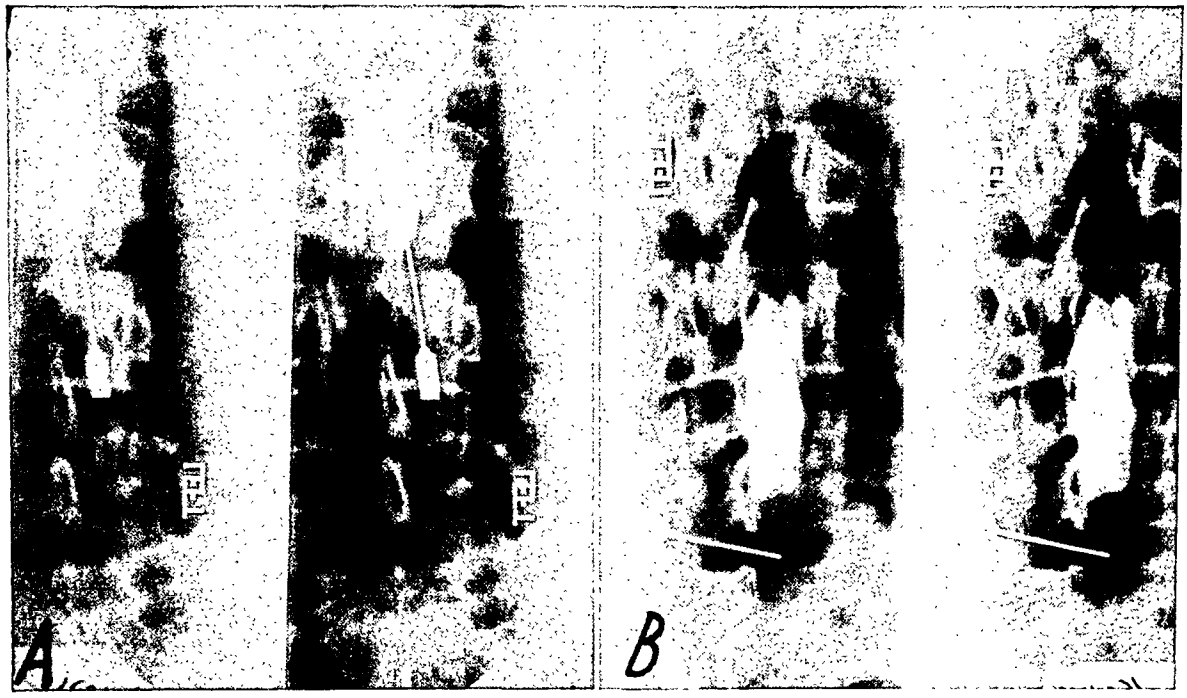


FIG. 4. Case IV. *A*, the upper margin of the block is situated at the level of the inferior margin of the body of the third lumbar vertebra. The dentate serrations and negative shadows due to swollen nerve roots are well visualized. *B*, the lower margin of the obstructive lesion is seen with the patient in the head-down position after the instillation of additional pantopaque into the caudal sac. Swollen nerve roots are seen in this region as well.

Plain roentgenographic examination of the lumbosacral spine showed straightening of the usual lumbar lordotic curve and slight arthritic changes in the lowermost two lumbar vertebrae. The intervertebral spaces were normal. A Schmorl's node was seen in the superior surface of the third lumbar vertebra.

Myelography after the injection of 3 cc. of pantopaque revealed a complete obstruction at the level of the inferior margin of the third lumbar vertebra. Several dentate small serrations were seen in the caudal end of the pantopaque column, and linear radiolucent streaks indicative of swollen nerve roots were present.

After removal of the pantopaque, a second spinal needle was inserted into the lumbosacral interspace. Manometric determinations at this site showed a partial block. On tilting the patient into the head-down position the lower margin of the blocking lesion was identified at the level about 1 cm. beneath the inferior margin of the fourth lumbar vertebra. Parallel radiolucent streaks indicative of swollen nerve roots were seen below the level of the block. No defects in the pantopaque column below the block were found. On completion of the examination the pantopaque was removed easily.

The protein content of the cerebrospinal fluid obtained from above the block was 120 mg. per 100 cc.

A laminectomy of the third and fourth lumbar vertebrae was performed. A large herniated disc was found anteriorly and above the interspace between the third and fourth lumbar vertebrae compressing the cord posteriorly. This was removed transdurally and the patient made an uneventful recovery.

Case v. B. F. (Hosp. No. 220577) female, aged thirty-three, had low back pain one year before admission without any known traumatic episode. During the past four months she had had a definite increase in libido. Eight days prior to admission numbness over the lower abdomen, buttocks, perineum and anterolateral aspects of both thighs appeared together with urinary retention requiring catheterization. Obstipation was present for eight days. She also had severe shooting pains down the posterior aspect of both thighs. A sensory level below the first sacral dermatome was elicited bilaterally. The left abdominal reflexes were slightly less active than the right and there was failure of the normal left plantar response. Both ankle jerks were diminished, the left more than the right. About 20 per cent impairment of motor power of the left lower extremity was present.

The clinical diagnosis was cauda equina tumor.

Plain roentgenograms showed no evidence of bony abnormality and the intervertebral spaces were normal.

Myelography after the instillation of 3 cc. of lipiodol between the third and fourth lumbar vertebrae showed a complete obstruction at the level of the superior aspect of the neural arch of the fifth lumbar vertebra. The caudal end of the sac was somewhat oblique, the right side being slightly lower than the left. The defect was rather smooth with a slight convexity in its midportion.

The cerebrospinal fluid proteins were 55 mg. per 100 cc., and the globulin was two plus.

A lumbosacral laminectomy revealed the dura corresponding to the first sacral segment to be covered with thickened ligamentum flavum. It was evident that the roots were riding high over an obstruction in the spinal canal. These were pulled aside and a very large protrusion through a much thinned anterior dura indicative of a herniated disc was observed. This was removed transdurally and the patient made an uneventful recovery.



Fig. 5. Case v. A somewhat oblique line of block is seen at the level of the neural arch of the fifth lumbar vertebra.

DISCUSSION

A total of 590 cases collected from the

literature examined by means of lumbar myelography, together with the 150 reported here, were reviewed to ascertain the relative incidence of complete spinal canal obstruction with protrusion of the lumbar discs.[1] This did not include series reported in which no cases of complete block were mentioned, a factor which reduces the absolute incidence of this condition. Only those in which the contrast medium was completely unable to traverse the region of block were included. Partial blocks, no matter how pronounced, and transverse defects were not considered within the scope of this presentation. All in all, 27 cases with complete block were found, an incidence of 3.3 per cent.

The longest series of such cases was that of Payne and French, who reported 8 cases out of 90 examined myelographically and verified at operation. The presenting symptoms in this group were chiefly low back pain with subsequent involvement of both legs. There was also weakness of the legs with sensory disturbances there and in the saddle area, urinary and bowel difficulties, muscular atrophy of the glutei, calf and thigh muscles and motor impairment and altered reflexes.

Ver Brugghen[2] reported 9 out of 300 consecutive patients with herniated discs presented symptoms of acute compression of the cauda equina. Myelographic examinations were not made in his series. Clinically the patients presented symptoms of severe sciatica, saddle anesthesia, weakness of the legs and sphincter disturbances. Ankle jerk and knee jerk reflexes were affected in most of his patients. Spinal taps in 3 patients showed complete block.

Hampton and Robinson also reported that complete block due to herniation of the lumbar intervertebral discs may simulate tumors of the cauda equina. Love and Walsh[3] mentioned that block is rare unless paraplegia is present. Arbuckle and Sheldon commented that herniation of the nucleus pulposus and cauda equina tumors may produce similar clinical syndromes which cannot be excluded one from the other on the basis of history and physical findings alone.

In contrast with these reports of severe neurologic disturbances are the first 4 patients in this series. While all had low back pain often aggravated by straining, this was quite variable and periods of remission were frequent. In some there was considerable doubt as to whether a tumor, a disc or for that matter any organic lesion was present. Sensory changes in the saddle area, urinary and bowel difficulties and abnormal plantar reflexes were observed only in the fifth patient diagnosed as having a cauda equina tumor. Absent ankle jerks bilaterally were present in 3, and the knee jerks were diminished bilaterally in one and unilaterally in another patient. Very little motor loss was noted except in the fifth patient. The duration of symptoms varied from three months to over twenty years. Four of the 5 had symptoms for less than two years.

Plain roentgenograms of the lumbosacral spine showed very little change from the normal. Slight arthritic changes were present in 2 patients, quite compatible with their ages. Narrowing of the lumbosacral interspace was present in 2 patients. The intervertebral spaces between the lower three lumbar vertebrae were diminished in 1, and 2 had normal intervertebral spaces. The sites of the herniations did not correspond with the narrowed discs. No changes in the pedicles, laminae or contours of the spinal canal were noted.

The most reliable objective evidence of herniation of the nucleus pulposus is obtained by means of pantopaque myelography. This procedure has a place of special importance in the diagnosis of complete block before the advent of signs of cauda equina compression. The identification of these patients is important, inasmuch as operative intervention removes the possibility of progressive changes. It becomes imperative, then, in selected patients to provide a diagnosis even in the absence of clinical changes of a classical nature. One must not be overenthusiastic

in selecting patients for myelography, but a certain judicial balance is necessary not to exclude certain individuals purely on the basis of underestimating their complaints.

The spinal puncture needle should be inserted between the third and fourth lumbar vertebrae if a low lesion is suspected, and the lumbosacral interspace utilized if there is any reason to suspect a higher site of rupture. In cases with complete block it may become desirable to utilize both sites. Thus, if a complete obstruction is encountered when the pantopaque is injected above the block, further examination is made by instilling an additional 2 cc. of pantopaque below the obstruction after removal of pantopaque from above the lesion. By proper manipulation of the patient on the tilting fluororoentgenographic table the upper and lower limits of the lesion can be identified. This procedure may also be of assistance in eliminating the possibility of double disc extrusions. Two such instances were encountered by Camp and Addington and overlooked because of lack of visualization of the caudal sac. Soule, Gross and Irving also mention this procedure, but do not describe instances of its application.

Before proceeding with myelography a specimen of fluid is withdrawn for total protein determination. Manometric readings made with the needle above the lesion obviously are of little value, and in all the cases reported here were normal. Partial or complete block was found in the 2 patients who had lumbar punctures at the lumbosacral interspace.

The protein content of the spinal fluid in the 5 patients reported here was elevated in 4 and normal in 1 case. The highest protein content was 175 mg. per 100 cc. The lowest, and only one within normal limits, was 29 mg. per 100 cc. French and Payne also observed elevated protein contents, in 1 case over 200 mg. per 100 cc. The importance of this lies in the evaluation of the significance of high proteins. Love[4] has stated that proteins over 100 mg. per 100 cc. are rarely associated with herniated discs, which is not in accord with the above observations.

Myelograms made after the injection of pantopaque above the lesion present a fairly characteristic appearance of the caudal end of the column, which is best seen with the patient in the erect position. In complete block due to extrusion of the nucleus pulposus there is a dentate, somewhat jagged appearance of the caudal end of the column with a transverse or slightly oblique line of block. Streaking of a linear radiolucent character parallel to the long axis of the spinal canal due to swelling of the nerve roots is frequent. This should be distinguished from dilatations of the pial veins which produce a convoluted defect corresponding with the displacement of the contrast medium by tortuous dilated venous channels.[5] The dentate appearance, in my opinion, is due to the compression of the nerve roots by the herniated disc.

The lower margin of the filling defect, as outlined by pantopaque after the instillation of 2 cc. below the lesion, is usually more irregular than the upper aspect and the dentate appearance is less pronounced. Edematous nerve roots may also be seen beneath the block.

Complete spinal canal obstruction frequently occurs with spinal cord tumors. About 20 per cent of these changes occur in the adjacent bony structures[6] and may be demonstrated on plain roentgenograms. Myelographically intramedullary tumors produce a caplike defect with streaks of oil to either side of the spinal canal for a variable distance alongside the tumor, and the axillary pouches along the course of the oil streaks stand out rather prominently.[7] Block due to extramedullary tumors usually reflect the contours of the tumor mass. In the case of perineurial fibroblastomas or neurofibromas this may assume concave filling defects, sometimes multiple and occasionally in the event of multiple tumors overlapping each other. Block due to a meningioma at the interspace between the twelfth thoracic and first lumbar vertebrae was mentioned by Arbuckle and Shelden.

and their illustration was hardly distinguishable from that of a protruded disc. I have observed similar patterns. However, meningiomas low in the lumbar canal are infrequent, and the site of block may prove of value in evaluating the underlying cause. Ependymomas of the cauda equina frequently produce pronounced bony changes with widening of the spinal canal and decalcification of the pedicles and laminae.

Complete block may also be produced by epidural abscess, as noted by Kaplan and Lautkin[8] and Maltby and Pendergrass. Obstruction secondary to metastatic malignancy, lymphomas or leukemia are usually accompanied by bony changes.

Differentiation between a high termination of the caudal sac and complete block at the lumbosacral interspace can be made with the patient erect. High termination of the caudal sac presents a tapered appearance narrowing to a blunt point, readily distinguished from the transverse dentate pattern present with block due to a herniated disc.

At operation it was found that all the discs reported here presented in the midline, similar to the others gathered from the literature. The operative approach, according to our neurosurgical colleagues, is best made transdurally in these cases. It is quite possible for even a large lesion to be overlooked in an extradural exploration, as was the case in 2 of the patients in this series. In these it was only after the dura had been opened and the region of the block thoroughly explored that a relatively small protrusion against the posterior spinal ligament was opened and large discs removed. The obvious inference is that an exploration cannot be considered complete in patients with midline disc herniations unless the dura is opened.

SUMMARY

Five patients with midline extrusion of the nucleus pulposus in the lower lumbar spine with complete spinal canal block are reported. The myelographic appearance associated with this condition when the pantopaque is instilled above the level of the lesion is a more or less transverse block with irregular dentate serrations at the caudal end of the column. When pantopaque is introduced beneath the level of the block the lower margin of the herniated disc is demonstrable as a somewhat more irregular transverse defect and the dentate serrations are less pronounced. This appearance is due to pressure of the herniated disc against the roots of the cauda equina.

Clinically the five patients reported here showed minimal neurologic changes in four and a syndrome diagnosed as cauda equina tumor in the fifth. Other cases gathered from the literature, which presented a similar myelographic pattern with the pantopaque injected above the block, were commonly associated with a more severe neurologic syndrome often indistinguishable from cauda equina compression due to tumor.

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THE ROENTGENOLOGIC DIAGNOSIS OF PROLAPSED GASTRIC MUCOSA*

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PROLAPSE of gastric mucosa into the duodenal bulb was first reported in 1911 by von Schmieden.[33] Since that time less than 50 cases have been reported which were uncomplicated by other coexistent abnormality in the stomach or duodenum; of these, 30 were proved by surgery or autopsy.

The diagnosis of gastric prolapse is a roentgenologic one. Rarely is it suggested by the clinician prior to gastrointestinal examination. We have found it difficult to evaluate the symptomatology since, in our experience, it is frequently discovered coincidentally with other pathological conditions which dominate the clinical picture.

The correct roentgenologic diagnosis of this condition is important since it is frequently mistaken for other more serious diseases.

ETIOLOGY

The etiology of gastric prolapse is as yet undetermined. Rees[27] believes that pyloric narrowing and subsequent hyperperistalsis loosens the mucous membrane and causes it to hypertrophy and prolapse. There was no evidence of pyloric narrowing in our cases. Eliason and Wright[10] propose the theory that a low grade inflammation of the mucosa results in its hypertrophy; contractions of the stomach might then enlarge and lengthen the hypertrophic folds and peristalsis push them through the pylorus. Our pathological studies shed no light on this possible mechanism; 2 of our cases had microscopic examination and both showed evidence of inflammation, but 1 also had a peptic ulcer. Forssell[13] demonstrated that the muscularis mucosae forms a special contractile organ of the mucous membrane and is able to displace the mucous membrane in all directions. Golden[14] described the following changes in the mucous membrane during "antral systole": Normally, by a cephalad movement of the mucous membrane, the mucosal folds change from a transverse direction to a longitudinal one. He believes that if this fails to occur, the transverse folds may be forced into the pylorus during peristalsis. Scott[31] believes that the structural conditions necessary for the development of prolapse are inherent in the walls of the normal stomach, but that prolapse occurs only after the fibers in the flexible submucosa have been stretched and loosened by abnormal gastric peristalsis, which, in turn, is initiated by neurogenic and/or chemical stimuli. He believes that certain neurogenic factors are the exciting causes of a disturbed gastric function which ultimately brings about a mucosal prolapse.

INCIDENCE

Scott[31] saw 14 cases of gastric prolapse in 1,346 upper gastrointestinal series in a one year period at a naval hospital. There were 325 duodenal ulcers, 13 gastric ulcers and no gastric tumors seen during that time. He feels that gastric prolapse occurs more frequently than is generally recog-

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nized, and may be overlooked because the examiner is not thinking of it, confuses it with other pathology, or recognizes but does not report it.

In a twelve month period from August, 1946 to August, 1947, there were 14,809 admissions to the Cincinnati General Hospital, and 10,000 new patients were seen in the out-patient department. The Department of Radiology did 1,257 upper gastrointestinal studies, and 35 cases of gastric prolapse were found. This represents an incidence of 2.8 per cent of all upper gastrointestinal series performed. In the same period 143 duodenal ulcers, 35 gastric ulcers, 30 gastric malignancies and 5 cases of antral gastritis were seen. Duodenal ulcer was approximately four times as common as gastric prolapse; gastric ulcer, malignancy and prolapse occurred with about equal frequency.

Scott's patients were in a younger age group than ours. The incidence of duodenal ulcer in his cases was much higher, but the relative incidence of gastric prolapse and gastric ulcer was approximately the same, just as in our series.

Of our 35 cases, 24 were males and 11 females; 25 were white and 10 colored. The ages of the patients varied between twenty-four and eighty-two, the average age being fifty-two years.

PATHOLOGICAL FINDINGS

Two cases were proved at autopsy and 1 following subtotal gastric resection for prepyloric ulcer. In these 3 cases the gastric mucosa slid easily over the muscularis and could be lifted through the pylorus for distances of as much as 2.5 cm. (Fig. 2).

Scott states that in 126 normal stomachs at postmortem examination it was impossible to pull the gastric mucosa through the pylorus. Bralow and Melamed[6] examined several normal stomachs within three hours postmortem and found that a small amount of gastric mucosa could be pulled through the pylorus, simulating a slight prolapse.

The 3 cases proved by pathological examination are briefly presented:

CASE REPORTS

CASE 1. S. F., a colored male, aged sixty-four, was admitted October 3, 1946. A diagnosis of carcinoma of the lung was established. An upper gastrointestinal series revealed only gastric prolapse (Fig. 1). Gastroscopy was performed twice, but the antrum was never visualized. The patient died on November 18, 1946.

The gross pathologic diagnoses were: carcinoma of the lung with widespread metastases;



FIG. 1. Case 1. (S. F.) The base of the duodenal bulb is concave. The deformity is produced by prolapsed gastric mucosa, recognized as negative linear filling defects passing through the pylorus into the bulb. This was confirmed at autopsy.

prolapse of gastric mucosa. The pathological description of the stomach by Dr. Paul Jolly follows: "The stomach is opened along the lesser curvature to a point 4 cm. proximal to the pylorus. With one finger in the duodenum and one finger in the stomach, a flap of gastric mucosa is found in the prepyloric region of the stomach which can easily be pushed back and forth through the pylorus. The stomach and duodenum are then completely opened. The rugae in the distal 15 cm. of the stomach lie in a circular pattern rather than in the usual longitudinal pattern. The mucosa appears quite redundant

and there is a fold of mucosa just proximal to the pylorus which is about 1.5 cm. high. This is easily moved back and forth through the pylorus, the maximum excursion of the free border of this fold being 2.5 cm. (Fig. 2). At a point 5 cm. proximal to the pylorus, the mucosa is easily pulled up into a fold 2.5 cm. high and in so doing the prominent fold at the pylorus is obliterated. The remainder of the gastroenteric tract presents no abnormality either in mucosa, wall or serosa."

Review of the microscopic sections of the stomach by Dr. Edward A. Gall revealed moderate infiltration of the mucosa with plasma cells and lymphocytes.

CASE II. J. B., a white male, aged seventy-four, was admitted to the hospital March 17, 1947, complaining of "swollen stomach," loss of appetite, cramping abdominal pain and diarrhea. A diagnosis of cirrhosis of the liver was made. Barium enema was negative. Examination of the upper gastrointestinal tract revealed esophageal varices and gastric prolapse (Fig. 5, *D*). The patient died on March 29, 1947. The gross pathologic diagnoses were: portal cirrhosis with hemorrhage from ruptured esophageal varices; gastric prolapse. The stomach was dilated with gas and a moderate amount of old bloody fluid. The mucosa was dark red. In the pyloric portion the mucosa was redundant and slid easily through the pylorus into the duodenum for a distance of over 2 cm. There was no gross evidence of inflammatory change. No microscopic sections of the stomach were made.

CASE III. G. C., a colored male, aged fifty-eight, was admitted to the hospital September 10, 1946, with a history of intermittent epigastric pain for several years, occasional hematemesis and tarry stools. Upper gastrointestinal studies revealed a prepyloric ulcer and gastric prolapse (Fig. 3). A gastric resection was advised because of the long history and numerous episodes of bleeding. On September 26, 1946, a subtotal gastrectomy was performed. The resected specimen consisted of a segment of the stomach and duodenum measuring 20 cm. in length. On opening the stomach, two ulcers were found on the distal portion of the posterior wall of the antrum, 2.5 cm. apart, each measuring 0.5 cm. in diameter. The pyloric mucosa was redundant and could be lifted through the pylorus for a distance of 2 cm. Microscopic sections (reviewed by Dr. Edward A. Gall) showed ulceration extending into the muscularis. Surrounding the ulceration there was acute and chronic inflammatory reaction. Sections elsewhere in the stomach revealed chronic inflammation within the mucosa and submucosa. Diagnoses of benign peptic ulcer and subacute and chronic follicular gastritis with erosion were made.

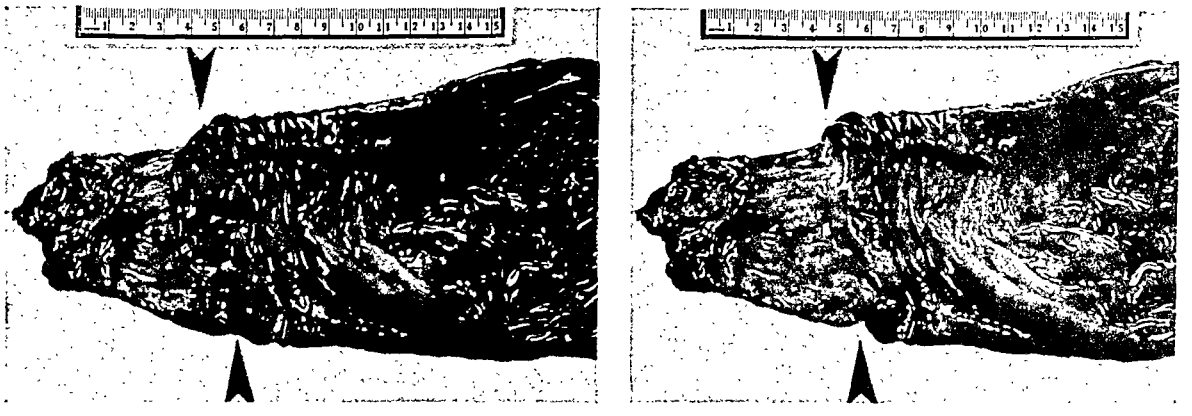
Gastroscopy was performed in 10 of the 36 patients by Drs. Leon Schiff, Carl Kumpe and Stuart Safdi. Prolapse of the gastric mucosa into the pylorus was actually visualized in 2 of the cases. In 7 cases the gastroscopist reported a normal stomach, although in several the antrum was not visualized. One case showed an atrophic gastritis.

SYMPTOMATOLOGY

In an effort to determine whether prolapse produces a characteristic symptom complex, we have divided the 35 cases into two groups: Group 1 (9 cases) had no clinical, laboratory or roentgenologic abnormality except prolapse. Group 2 (26 cases) had abnormal roentgen, clinical or laboratory findings in addition to gastric prolapse.

Brief histories of the 9 cases in Group 1 are presented:

CASE IV. M. C., a white female, aged thirty, was admitted to the hospital October 28, 1946, with a history of constant right upper quadrant pain for one week. There had been some anorexia and nausea, but no vomiting. There had been no hematemesis or melena. Bowel movements were normal. There was no history of food intolerance. Her previous health had always been good. Physical examination revealed only slight right upper quadrant tenderness. Hemoglobin was 12.6 gm. Kahn reaction was negative. A clinical diagnosis of acute hydrops of the gallbladder was made. Oral cholecystogram revealed a normally functioning gallbladder with no evidence of stone. Two barium enemas were negative. An intravenous pyelogram showed normal kidneys. Upper gastrointestinal series revealed gastric prolapse; there was no gastric residue at six hours. She was treated palliatively. The pain gradually subsided and she was discharged, asymptomatic, on November 16, 1946. No definite clinical diagnosis



A *B*

FIG. 2. Case 1. (S. F.) Autopsy specimen of antrum and duodenal bulb. Arrows indicate the proximal end of the pylorus. *A*. The mucosa has been lifted through the pylorus into the duodenal bulb for a distance of 2.5 cm., reproducing the condition recognized roentgenologically during life as gastric prolapse. *B*. The prolapsed gastric mucosa has been reduced.



Fig. 3. Case III. (G. C.) "Mushroom" appearance of the bulb due to gastric prolapse. The deformity in *B* might be confused with a polypoid lesion of the bulb. However, in prolapse the appearance of the bulb is constantly changing. Prolapse was confirmed at surgery. The two prepyloric ulcers found at operation are not well shown on these roentgenograms.

was established. She has not returned to the hospital since her discharge.

Case V. W. McK., a colored male, aged fifty-one, entered the clinic in January, 1947, complaining of dyspnea, "sour stomach," heart burn, gas and occasional vomiting for several years. Soda relieved these symptoms. He had been unable to eat fatty foods for years. He had had no episode of hematemesis or tarry stool. Except for moderate consumption of alcohol, the past history was not remarkable. The only positive findings on physical examination were obesity and some elevation of the systolic blood pressure. A clinical diagnosis of peptic ulcer was made. Hemoglobin was 12 gm. Kahn reaction was negative. Electrocardiogram was normal. Cholecystogram demonstrated a normally functioning gallbladder. Roentgenoscopy and roentgenography of the heart revealed cardiac enlargement which was predominantly left ventricular. Upper gastrointestinal studies demonstrated only gastric prolapse; there was no residue in the stomach at six hours. He was



Fig. 4. *A*, Case XIV. (I. L.) Typical "mushroom" appearance of the bulb due to a moderately large gastric prolapse.

B, Case XIII. (L. B.) Marked concavity of the base of the bulb due to a large gastric prolapse. This patient also had a pedunculated gastric polyp (arrow) which moved about freely in the stomach and was seen to prolapse into the bulb. The findings were confirmed by gastroscopy.

treated with belladonna, cremalin and a bland diet. At his last visit to the clinic in May, 1947, his symptoms were much improved.

CASE VI. R. B., a white male, aged thirty-eight, was admitted to the hospital on January 31, 1947. One year before, he had experienced an attack of epigastric pain lasting several days and requiring morphine for relief. Following this he was in good health until three months before admission when he had another episode of epigastric pain. The pain again subsided, and he was free of symptoms until eight days prior to admission when the same pain recurred. It was gnawing, intermittent, localized to the epigastrium, and unrelated to food. His physician prescribed cremalin, but this brought no relief. There was some relief with milk. Several days before admission he had had three teeth extracted following which persistent oral bleeding occurred. Several hours before admission he vomited a moderate amount of old blood. Past history revealed the patient to be a heavy drinker, consuming up to a pint of whiskey a day for years. Physical examination revealed only epigastric tenderness and some rigidity. It was not determined whether the vomited blood was coming from a gastric lesion or had been swallowed. A tentative diagnosis of bleeding peptic ulcer was made. Hemoglobin was 16.0

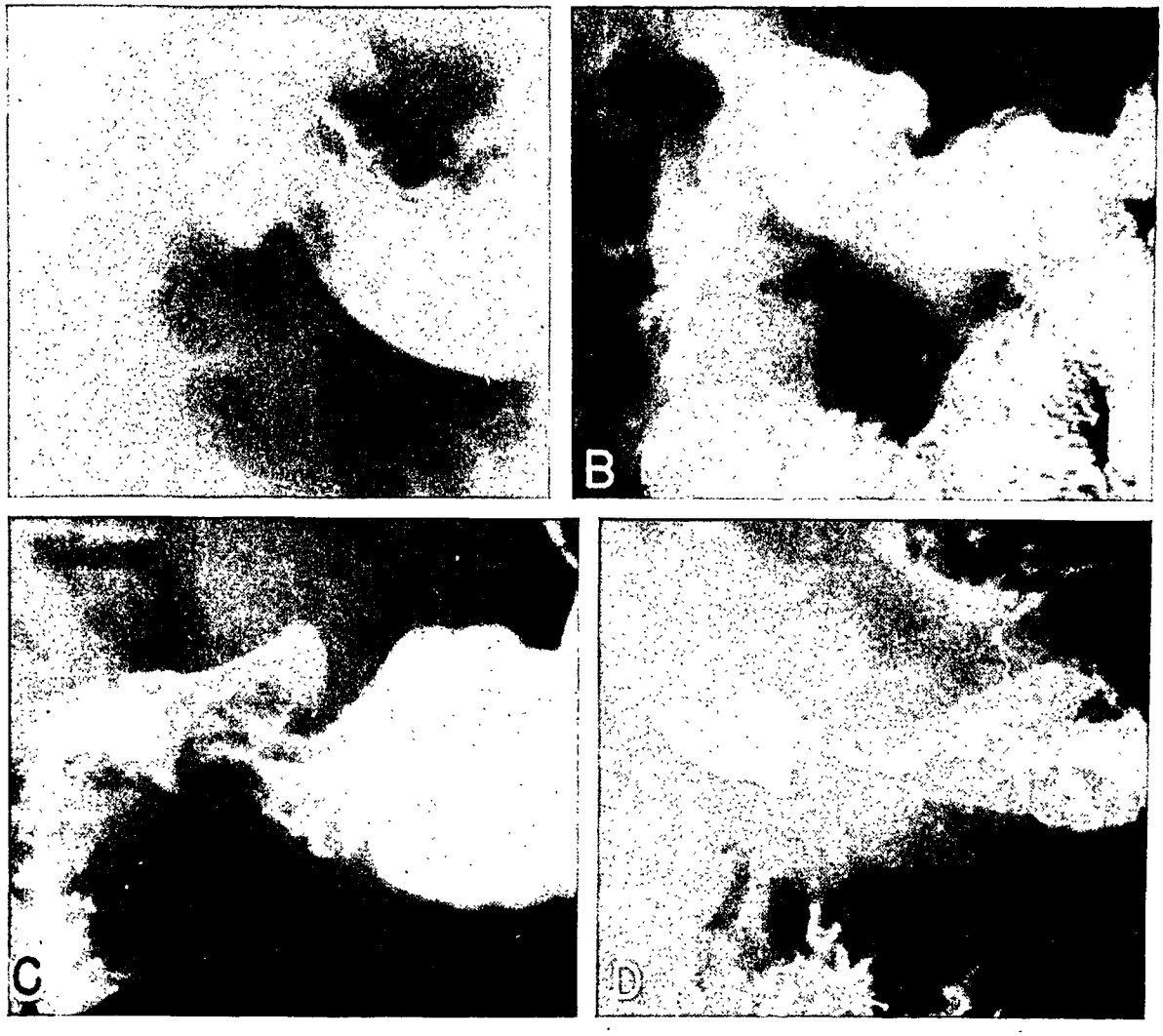


FIG. 5. *A* and *B*, Case XV. (W. A.); *C*, Case XVI. (M. G.), and *D*, Case II. (J. B.) Three cases demonstrating gastric mucosal folds passing into the duodenum. The folds are visualized as negative linear filling defects between the thin lines of barium. In the case illustrated in *D* (Case II) prolapse was confirmed at autopsy; the redundant gastric mucosa in the antrum was easily lifted through the pylorus for a distance of approximately 2 cm.

gm. Kahn reaction was negative. Electrocardiogram was normal. Two upper gastrointestinal studies were done. Both revealed gastric prolapse (Fig. 7) with no gastric retention at six hours. The patient was put on a Sippy diet, antacids and antispasmodics. His improvement was rapid and he was discharged, asymptomatic, on February 7, 1947. He has not returned.

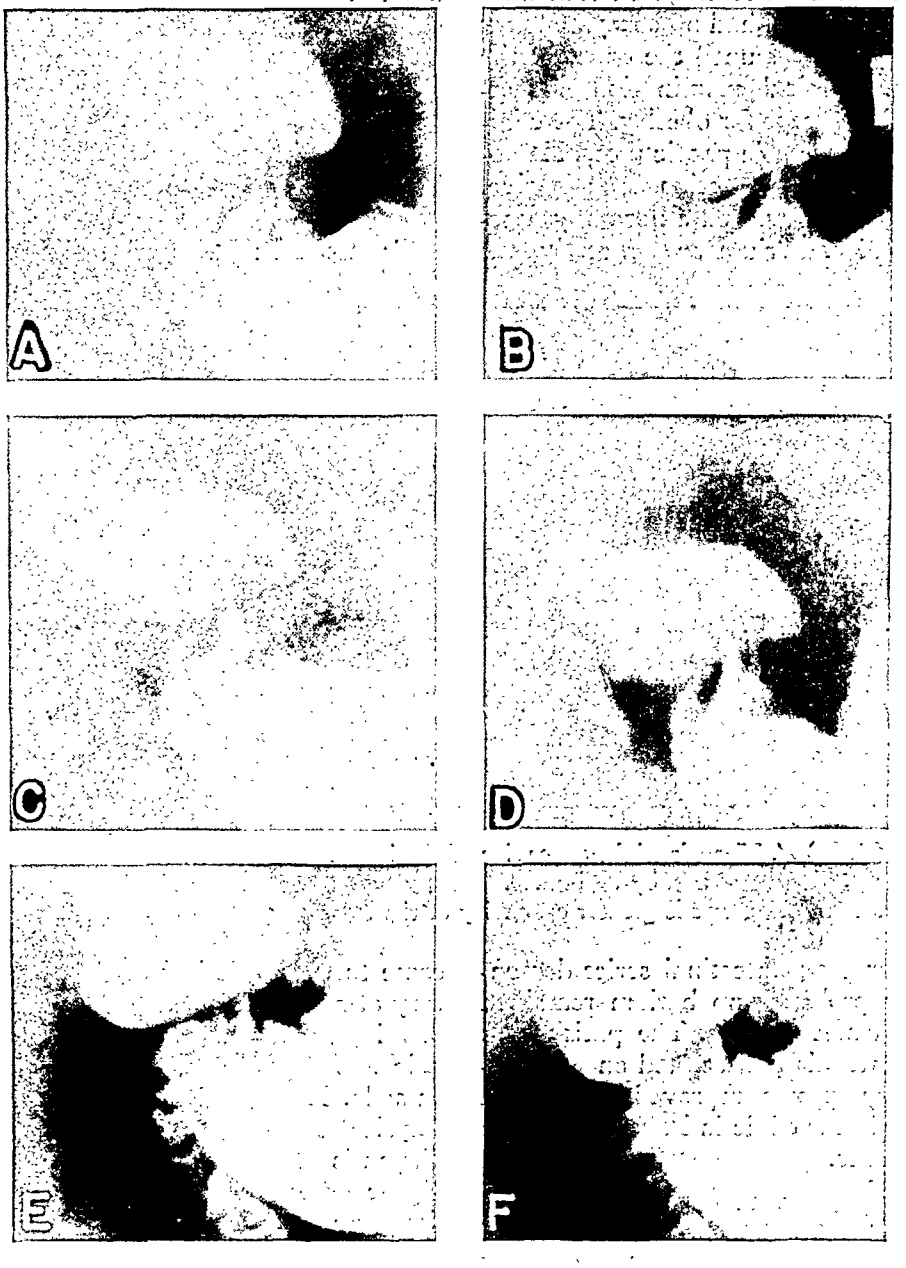


FIG. 6. Case XVII. (H. McK.) Roentgenograms taken in rapid succession with multigraph spot device. *A*, *B*, *C* and *D*, concavity of the base of the bulb due to prolapse. Gastric mucosal folds can be traced through the pylorus. *E* and *F*, prolapse is reduced. Bulb now appears normal.

CASE VII. A. F., a colored female, aged forty-three, came to the clinic in February, 1947, complaining of nausea, vomiting, and intermittent attacks of sharp epigastric pain for the past ten years. She denied hematemesis or melena. In 1938 she was discovered to have late syphilis following which she received adequate treatment. In 1946 the patient was admitted following an acute attack of severe upper ab-

dominal pain and vomiting. At that time she was thought to have mechanical small bowel obstruction. She was treated expectantly, the symptoms rapidly disappeared, and she was discharged with no definite diagnosis four days after admission. She had had no complaints for the past several months until the onset of the present illness. Physical examination was essentially negative except for obesity. The clinical diagnosis was probable peptic ulcer. Hemoglobin was 15 gm. Kahn reaction was negative. Oral cholecystogram revealed a normally functioning gallbladder. Barium enema study was negative. Upper gastrointestinal series demonstrated gastric prolapse; no barium remained in the stomach at six hours. The patient was treated with antacids and started on a reduction diet. Her symptoms improved rapidly and when last seen in the clinic in March, 1947, she was asymptomatic.

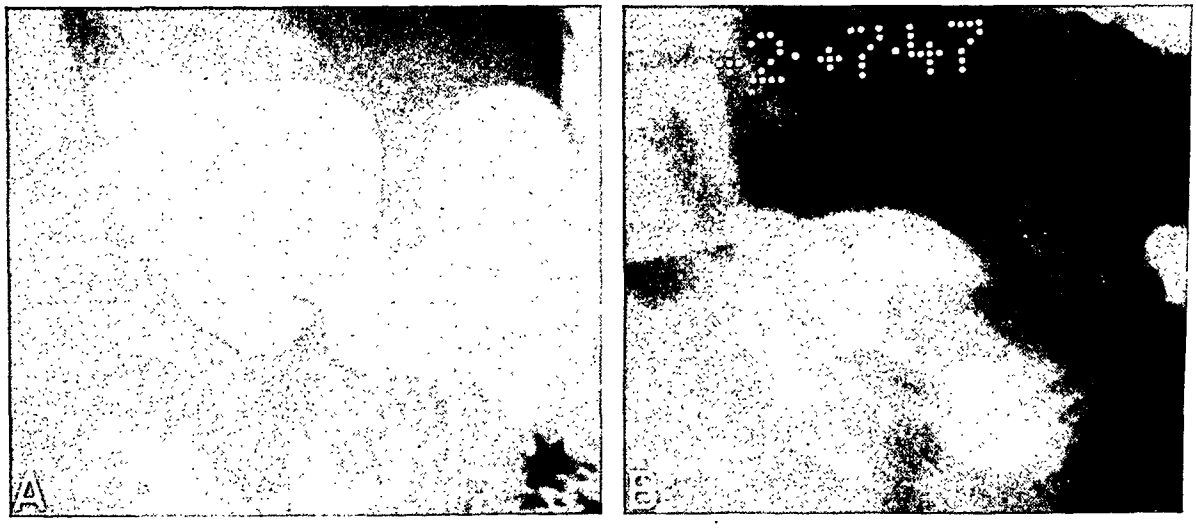


FIG. 7. Case VI. (R. B.) *A*. There is slight concavity of the base of the bulb. Gastric rugae passing through the pylorus are partially obscured by barium. *B*. Roentgenogram taken several minutes later. Appearance of the bulb has changed. There is greater concavity of the base.

CASE VIII. G. D., a white male, aged forty-one, visited the clinic in March, 1947, with a history of recurrent episodes of epigastric pain for one year. They occurred when the stomach was empty and were relieved by food, milk and antacids. The pain never awakened the patient at night. He experienced occasional nausea and vomiting but no hematemesis or tarry stools. Fried foods precipitated his symptoms. The patient was a known chronic alcoholic. Physical examination was normal except for slight epigastric tenderness. The clinical diagnosis was probable peptic ulcer and chronic alcoholism. Hemoglobin was 15.5 gm. Three upper gastrointestinal series were done at monthly intervals and gastric prolapse was found (Fig. 8, *E* and *F*). On no examination was there a six hour gastric residue. The clinician stated that he believed this patient's symptoms were due to gastric prolapse. He was treated with a Meulengracht diet, belladonna and cremalin. His symptoms improved and when last seen in the clinic in June, 1947, he had no complaints.

CASE IX. R. H., a white male, aged forty, came to the clinic in March, 1947, with a history of nausea, vomiting and recurrent attacks of mild epigastric pain for several years. The pain was in part relieved after ingestion of food or soda. He denied hematemesis and melena. Physical examination was entirely negative. A diagnosis of probable peptic ulcer was made. Upper gastrointestinal series revealed gastric prolapse; no barium was seen in the stomach at six hours. He was put on a regimen of bland diet and amphogel. He was last seen in the clinic in April, 1947, at which time his symptoms had improved.

CASE X. F. P., a white male, aged forty-three, was first seen in April, 1947, complaining of intermittent attacks of epigastric distress, nausea and vomiting for several years. The distress was worse at night when his stomach was empty. It was relieved by food, milk and soda. He had

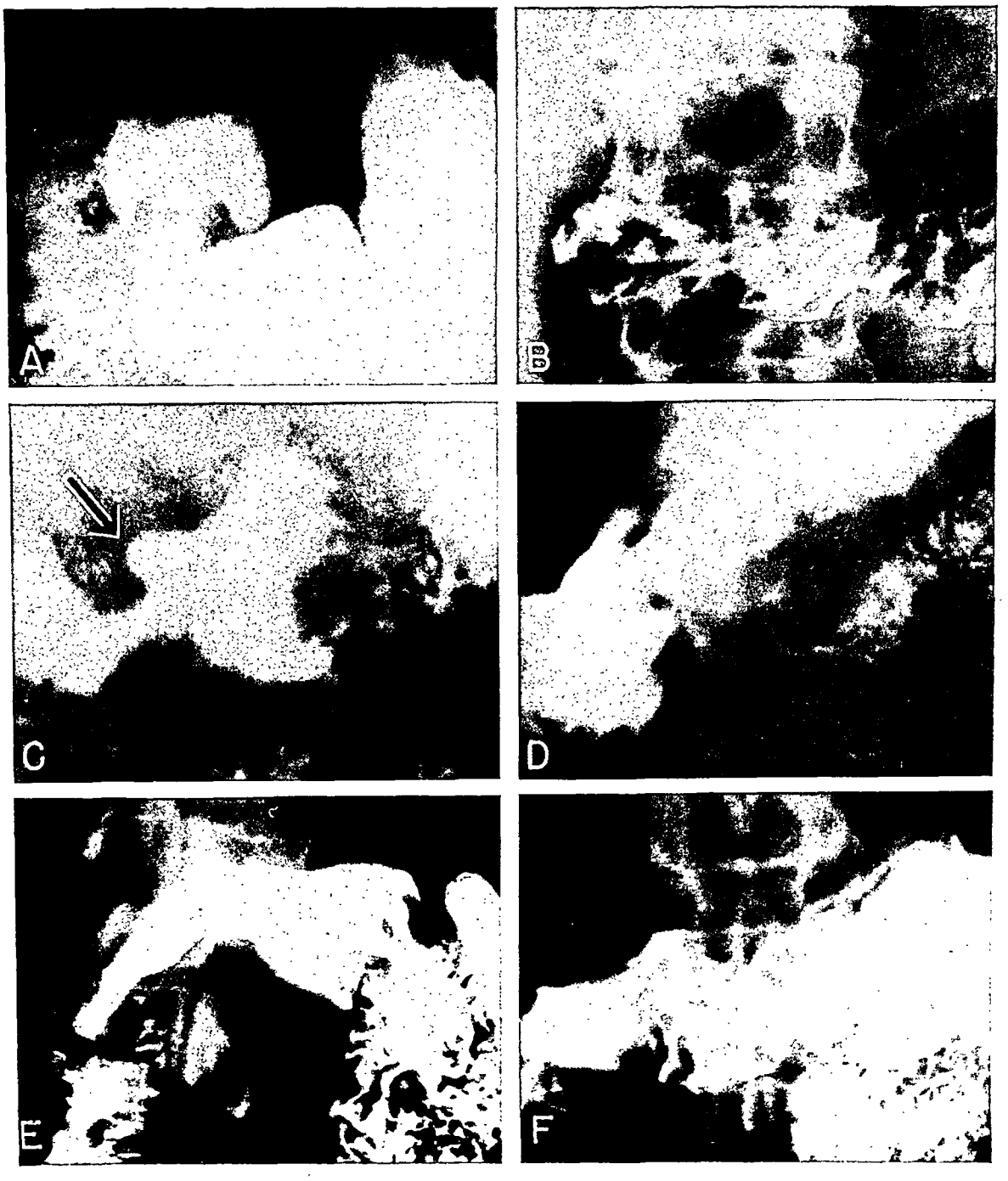


Fig. 8. *A* and *B*, Case xviii. (I. T.) In *A*, gastric mucosa is prolapsed into the bulb producing a "mushroom" appearance. *B* demonstrates the reduced phase. Redundant mucosal folds are piled up in a transverse direction in the antrum. *C* and *D*, Case xix. (R. T.) In *C*, gastric folds are passing through the pylorus and into the duodenum. There is slight concavity of the base of the bulb. An ulcer niche (arrow) is demonstrated at the apex of the bulb. In *D* the prolapse is almost completely reduced, and redundant gastric mucosa has assumed a transverse position in the antrum. *E* and *F*, Case viii. (G. D.) In *E*, there is slight concavity of the bulb due to prolapse. In *F*, the prolapse is reduced; gastric mucosa is piled up in transverse folds in the distal portion of the stomach.

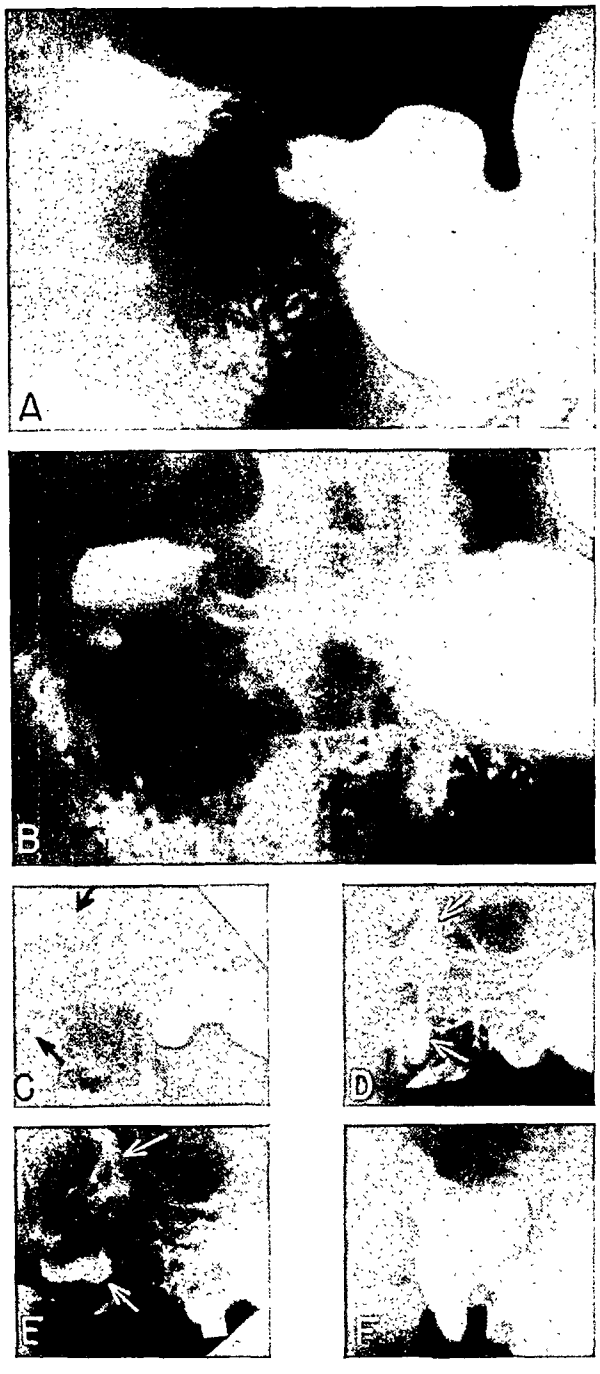


FIG. 9. *A* and *B*, Case IV (M. D.) In *A*, gastric mucosa passes into the duodenum producing slight concavity of the bulb. In *B* prolapse is reduced; gastric folds assume a horizontal position. *C*, *D*, *E* and *F*, Case XX (C. R.) Roentgenograms taken in rapid succession with the multigraph spot device. Arrows indicate base of bulb. In *C*, gastric rugae pass into the duodenum causing concavity of the base of the bulb. In *D*, the prolapse is reduced; gastric folds lie in a horizontal position in the antrum. In *E* and *F*, there is beginning invagination of gastric mucosa with some concavity of the base of the bulb.

never had hematemesis or tarry stools. Physical examination was normal. A diagnosis of peptic ulcer was made. On examination of the upper gastrointestinal tract, gastric prolapse was demonstrated. There was no gastric retention at six hours. The patient was treated with belladonna and a bland diet and was asymptomatic within one month. When last seen at the hospital in July, 1947, he had no complaints.

CASE XI. J. F., a colored male, aged forty, visited the clinic in May, 1947, with a history of intermittent pain in the upper abdomen, worse at night, for the past year. He had had much belching but no nausea, vomiting or tarry stools. Past history was non-contributory. Physical examination was not remarkable. A clinical diagnosis of peptic ulcer was made. Hemoglobin was 15 gm. Kahn reaction was 4 plus. Upper gastrointestinal studies revealed gastric prolapse. There was no gastric residue at six hours. The patient was treated with antacids and antispasmodics and was given antiluetic therapy. At his last visit to the clinic in July, 1947, he had been symptom free for three weeks.

CASE XII. E. S., a white male, aged twenty-nine, came to the clinic in June, 1947, complaining of epigastric discomfort, nausea and occasional vomiting for ten years. He obtained relief from these symptoms with food and soda. There was no history of hematemesis or melena. He was a known chronic alcoholic. Two years ago his family physician told him that he had a duodenal ulcer. He was followed in the psychiatric clinic in 1946 with a diagnosis of anxiety neurosis with paranoid trends. Except for slight epigastric tenderness, the physical examination was not remarkable. The clinical diagnosis was peptic ulcer. Hemoglobin was 14.5 gm. An upper gastrointestinal series revealed only gastric prolapse; no gastric residue was seen in the stomach at six hours. The patient was treated with belladonna, cremalin and Meulengracht diet. He was last seen in the clinic in the latter part of July, 1947, and felt much improved.

These 9 patients present quite similar clinical pictures. The commonest complaint was recurrent attacks of epigastric pain or distress, often relieved by food, milk or alkalies. This occurred in 8 of the 9 patients. Nausea, vomiting, gas and belching were frequent symptoms. Two patients com-

plained of intolerance to fried or fatty foods. In most cases the symptoms began at least one year prior to roentgen examination.

In only 1 patient was there hematemesis (Case VI). However, this patient had had dental extractions just prior to admission and it was believed that the hematemesis probably resulted from swallowed blood.

In no case was an abnormally low hemoglobin found. Hematemesis, melena and secondary anemia in association with prolapse have been reported frequently in the literature.[3,5,9,21] They were not present in the uncomplicated cases in our series.

Four of the 9 patients in Group 1 were consumers of alcohol, and 3 of these were classified as "heavy drinkers."

Four patients had some degree of epigastric tenderness.

The diagnosis prior to roentgen study in 8 of the 9 patients was peptic ulcer; in the ninth, hydrops of the gallbladder was suspected.

The similarity of the symptoms in these 9 patients, and the absence of any other findings which might explain them, leads one to suspect that they might have been produced by gastric prolapse. A number of cases reported in the literature presented clinical histories not unlike those in our 9 patients. However, the evidence is still inconclusive, and for the present we cannot be certain that gastric prolapse is a clinical entity.

Treatment of the patients in Group 1 was medical; bland diet, antacids and antispasmodics were prescribed. In every case there was improvement. Several patients were asymptomatic within one month. However, follow-up has been for a relatively short period of time. There is no apparent explanation for the symptomatic relief from these measures. Scott also advocates sedation and states that freedom from tension, strain, fear and worry (factors which might produce disturbed gastric function) brings improvement. The literature refers frequently to the surgical treatment of prolapse.[2,19,22,24,25,26] McKenzie believes the indications for surgery are threefold: (1) equivocal roentgen signs of prolapse from which a lesion necessitating operation (e.g. a neoplasm) cannot be definitely differentiated; (2) continued bleeding; (3) evidence of pyloric obstruction. In none of our cases was surgery deemed necessary.

Table 1 lists the coexistent conditions found in the 26 cases in Group 2. In several patients more than one other abnormality was discovered. Because the other processes frequently dominated the clinical picture, no effort has been made to evaluate what part prolapse might have played in production of symptoms or signs in these cases.

TABLE I

COEXISTENT CONDITIONS FOUND WITH GASTRIC PROLAPSE IN 26 PATIENTS

Condition	No. of Cases
Diverticula of colon	5
Duodenal ulcer	3
Cirrhosis of liver	3
Heart disease	3
Non-functioning gallbladder	2
Gastric ulcer	2
Probable gastric polyp	2
Carcinoma of lung	2
Carcinoma of ovary	1
Carcinoma of colon	1
Carcinoma of pancreas	1
Foreign body in colon	1
Esophageal varices	1
Polyp of colon	1
Antral gastritis	1
Pedunculated, prolapsing gastric polyp (confirmed by gastroscopy)	1

ROENTGEN FINDINGS

The roentgen findings in gastric prolapse are as follows:

1. There is inconstant deformity of the duodenal bulb. The bulb assumes a "mushroom" appearance, with concavity of the base, when gastric mucosa is invaginated into it (Fig. 4).

2. Mucosal folds are seen passing from the stomach into the duodenum (Fig. 5).

They are visualized as multiple negative linear filling defects. A single rugal fold may normally pass through the pylorus, and this must not be mistaken for prolapse.

3. The appearance of the bulb varies as the gastric mucosa slides back and forth through the pylorus (Fig. 6 and 7).

4. When the prolapse is temporarily reduced, redundant mucosa may pile up in the antrum assuming a circular or transverse direction rather than the usual longitudinal one (Fig. 8); or, it may assume a horizontal direction and appear normal (Fig. 9). During the reduced state there is no deformity of the bulb.

5. Peristaltic waves pass through to the pylorus normally.

6. There is usually no narrowing or elongation of the pyloric channel.

7. The size of the folds is normal.

8. No ulcer niche is demonstrable in the pylorus or duodenum.

9. There is no irritability of the duodenal bulb.

10. Although there is frequent reference to gastric retention in the literature[4,9,26] in none of our cases in Group 1 was this seen.

The importance of prolapse lies in its differentiation from other more serious pathology. In one of our cases the roentgen findings were at first erroneously interpreted as duodenal ulcer. On re-examination, prolapse was recognized as the cause of deformity of the bulb.

DIFFERENTIAL DIAGNOSIS

1. Carcinoma of the antrum: There is a constant deformity of the antrum, and the rugal pattern is usually destroyed. Peristalsis is altered or absent in the involved area. Rarely is the duodenal bulb affected. A mass may be palpable.

2. Duodenal and pyloric ulcer: The ulcer niche is often demonstrable. In duodenal ulcer there may be irritability and spasm of the bulb with resultant constant deformity; the prepyloric folds are normal. In pyloric ulcer the mucosal folds about the involved area may be distorted and peristalsis may not pass through them. No gastric rugae can be demonstrated passing through the pylorus. There is often a six hour gastric residue as a result of pyloric obstruction.

3. Hypertrophic pyloric stenosis in adults:[1,8,18] This condition is characterized by an elongated, narrowed pyloric channel, often with an excentric axis. Occasionally a narrow crevice or rounded depression is demonstrated at the midpoint of the lower border of the canal, resembling a niche. There is concavity of the base of the bulb (similar to that seen in prolapse) which, according to Kirklin and Harris,[18] is due to partial invagination of hypertrophied muscle into the duodenum and is an important diagnostic criterion of this condition. However, the defect is constant, and rugae cannot be traced into the base of the bulb.

4. Antral gastritis: The rugae in the distal portion of the stomach are swollen, thickened and coarse.[11] Cole[7] describes their appearance as similar to "night crawlers." They may produce a constant filling defect in the antrum through which peristalsis may or may not pass.[32] The pyloric channel may be narrowed. However, the bulb is normal, facilitating differentiation from gastric prolapse.

5. Duodenal polyp or papilloma:[30,34] This rare condition[15,16,23] produces a constant vacuolated or multilocular smooth filling defect in the bulb. The pylorus appears normal and gastric rugae cannot be traced through it.

6. Benign gastric tumors: These are rare.[12,25,28] They may be visualized as radiolucent filling defects surrounded by intact mucosa through which peristalsis passes normally. Rugae in the antrum appear normal and there is no deformity of the bulb. In such instances differentiation from prolapse is not difficult. However, gastric tumors may be pedunculated and prolapse into the bulb,[20] or they may slide through the pylorus on prolapsing gastric mucosa. Differentiation in such cases is difficult.[9] Rubin[29] describes a case diagnosed preoperatively as prolapsed gastric mucosa, but at surgery prolapsing gastric polyposis

with carcinomatous degeneration was found. Appleby[2] cites a similar case. There is frequently obstruction in these cases and six hour gastric residue is common.

One confirmed case of prolapsing gastric polyp was seen in the Department of Radiology during the one year period of this study.

CASE XIII. L. B., a white male, aged eighty, was admitted to the surgical service with an infected abrasion of the right hand on February 10, 1947. He had multiple vague complaints. Physical examination was essentially negative. Kahn reaction was 3 plus. Two upper gastrointestinal roentgen series in March, 1947, revealed a gastric polyp measuring approximately 2.5 cm. in diameter arising just above the incisura of the stomach and apparently hanging from a pedicle. It moved freely about within the stomach and was seen to prolapse into the duodenal bulb several times. A large prolapse of gastric mucosa into the bulb was also demonstrated. On gastroscopy the polypoid lesion was seen projecting into the lumen of the stomach in the region of the antrum. It was constantly moving and on two occasions it swept through the pylorus accompanied by the redundant gastric mucosa. Due to the patient's age, operation was not advised. He was discharged on March 20, 1947, and has been followed in the clinic. At his last visit in July, 1947, he had no complaints referable to the gastrointestinal tract.

7. Duodenitis: This should offer no differential problem. Kirklin[17] describes the bulb as small, irritable and spastic, with coarse reticular mucosal pattern. There is irritability and distortion of the mucosa of the duodenum distal to the bulb occurs.

SUMMARY AND CONCLUSIONS

Prolapse of the gastric mucosa is not uncommon; thirty-five cases were seen in the Department of Radiology of the Cincinnati General Hospital in a twelve month period. The incidence was approximately the same as that of gastric ulcer. It was frequently discovered coexisting with other intra-abdominal pathology. In one-fourth of our cases in which no other abnormality was found, symptoms suggested peptic ulcer, and that diagnosis was made clinically in eight of the nine patients prior to gastrointestinal roentgen studies. That these symptoms were related to gastric prolapse is suspected, but this relationship has not been convincingly established. The roentgen findings in prolapse are diagnostic but must be differentiated from other more serious conditions. In our nine uncomplicated cases, medical treatment brought rapid improvement in symptoms.

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ARACHNODACTYLY (MARFAN'S SYNDROME)*

TWO CASE REPORTS WITH ETIOLOGICAL IMPLICATIONS

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RECENTLY Tobin and his associates[11] reported clinical data and complete data on the necropsies of 2 adults with arachnodactyly both of whom died as the result of a dissecting aneurysm of the aorta. In their report they reviewed the literature on this syndrome, stating that "Although over 200 cases of arachnodactyly have been reported, descriptions of only twelve autopsied are found in the literature, of these ten are more or less complete descriptions." They stated that the role of the endocrine glands, particularly the hypophysis, remains obscure.

It is the purpose of this paper to present 2 cases of arachnodactyly, one with dislocated lens, tremulous iris and an enlarged sella turcica; the second case had a small sella turcica and no dislocation of the lens. An explanation of the findings will be given.

In 12 autopsied cases of arachnodactyly as reported by Tobin and associates 10 had cardiac disturbances. Four had an increase in the eosinophil cells of the pituitary and the 2 reported by the Tobin group also had this same finding, making a total of 6 of the 14 autopsied cases. Of this total 4 pituitaries were reported as normal; one had a cyst of the gland and 3 had no report on the pituitary. Thus pathological lesions of the pituitary are a common finding.

Tobin stated that their 2 cases had a high arched palate the significance of which will be discussed later. They also stated that the jaw juts forward but the opposite is true in my 2 cases (Fig. 2 and 9).

CASE 1. The patient was a white six year old male of Italian parentage who was brought to the referring ophthalmologist, Dr. Ralph Pino, because of visual disturbance and failure of body development. He weighed 8 pounds and 7 ounces at birth (3.8 kg.). He talked at ten months, walked at fifteen months, and teeth first appeared at the age of three months. It was noted that his hands and feet were longer than normal. He had received roentgen therapy for an enlarged thymus at the age of two years. It was also noted at about the age of fifteen months that his back was not straight. Soon after birth it was noted that he perspired a great

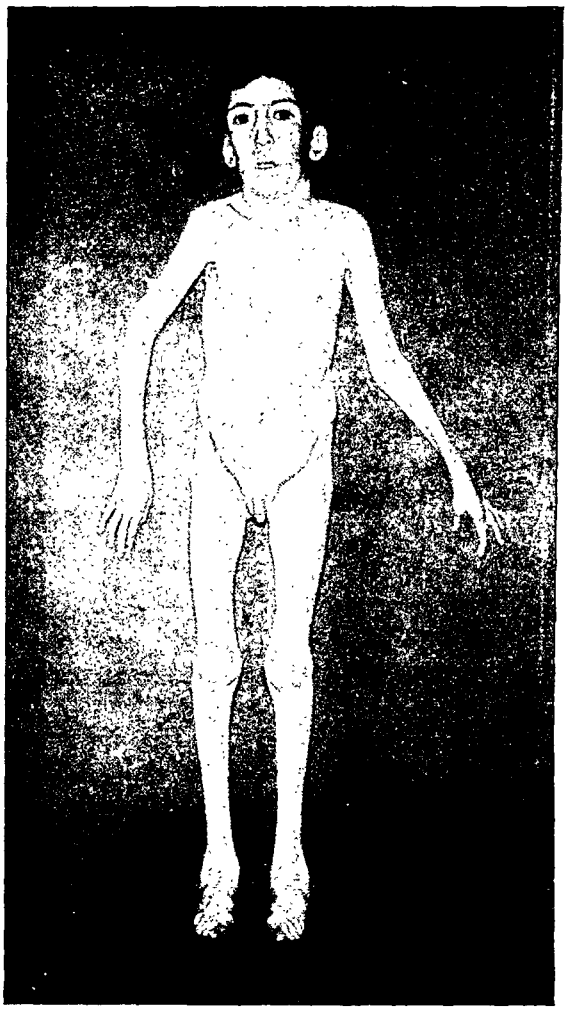


FIG. 1. Case 1. Front view showing the physical characteristics of arachnodactyly.

* From the Department of Medicine and Clinical Research, Harper Hospital.

deal. As he grew older the long spindly type of extremities developed; likewise the head assumed a dolicocephalic shape also characteristic of arachnodactyly.

Past History. At the age of two and a half years his tonsils were removed. He gave a history of measles, "strep throat" and "intestinal flu." He had been seen by two orthopedic surgeons because of the skeletal deformities. He was precocious in his learning. No rheumatic history was present.



FIG. 2. Case 1. Lateral view. The dolichocephalic head, winged scapulae, subluxated ankle joints are shown.

Family History. The father was living, his height was 68 inches (172.7 cm.) and he weighed 150 lb. (68.0 kg.). The mother was living; she was short and undernourished, the height being 61 inches (154.9 cm.) and she weighed 98 lb. (44.5 kg.). There was no familial history of arachnodactyly. The maternal grandmother had diabetes mellitus. A paternal cousin had epilepsy and another paternal cousin had strabismus. Of importance is the fact that both parents had a high arched palate as did the patient. There was no consanguinity in the parents.

Physical Examination. The patient was a slender boy with a marked dolicocephalic head (Fig. 1 and 2). The body measurements were as follows (normal measurements are given for comparison):

	PATIENT		NORMAL	
	inches	cm.	inches	cm.
Head	20.5	(50.8)	20.5	(50.8)
Chest	21.0	(53.34)	22.1	(55.88)
Waist	19.5	(48.26)	20.9	(53.34)
Span	47.0	(119.38)	44.0	(111.76)
Upper	24.0	(60.96)	24.0	(60.96)
Lower	22.5	(56.0)	21.0	(53.34)
Height	46.5	(116.96)	45.0	(114.30)
Weight	36 lb.	(16.3 kg.)	43.9 lb.	(20 kg.)

The referring ophthalmologist, Dr. Ralph Pino, reported as follows:

"From the eye standpoint this child has a dislocated lens that appears from a tremulous iris. We were not able to dilate the pupils sufficiently to make an intraocular examination that is satisfactory. It would appear that the luxation of the lens is not sufficiently marked to interfere too much with vision in this stage. As the child grows older I would anticipate there would be greater luxation." The external occipital protuberance and the supraorbital ridges were prominent. The eyes were prominent. The pupils were small. The ears were prominent and the lower lobes flared outward. The teeth were in only fair condition, several showed caries. Malocclusion with recession of the lower jaw was present. There was a high arched palate. The thyroid gland was palpable. The chest was deformed and the scapulae were of the winged type due to the poor musculature development. The spine showed scoliosis in the thoracic region. The heart was ptotic and there was a loud systolic murmur heard all over the precordium; this had its loudest intensity at the base of the heart. The pulmonic second sound was accentuated. The blood pressure was systolic 112, diastolic 66. The pulse rate was 74 and regular. The liver was not palpable. The genitalia were fairly well developed and both testicles were in the scrotum. The joints of the elbows, knees and ankles were enlarged. There was hyperextensibility of the elbows and knees. The extremities

were long and spindly in character. There was subluxation of the ankle joints. The fingers and toes were abnormally long. The musculature was poorly developed and hypotonic. There was a generalized absence of subcutaneous fat. The capillaries of the extremities were dilated and this gave them a bluish tinge. Some hirsutism of the arms and legs was present.

The urinalysis was normal. The hemoglobin was 80 per cent (12.5 gm.). There were 3,200,000 erythrocytes, 7,200 leukocytes with a normal differential count.

Roentgenograms were reported as follows:

Skull: The tables of the skull are relatively thin with a minimal amount of diploic structure. The anteroposterior diameter of the skull

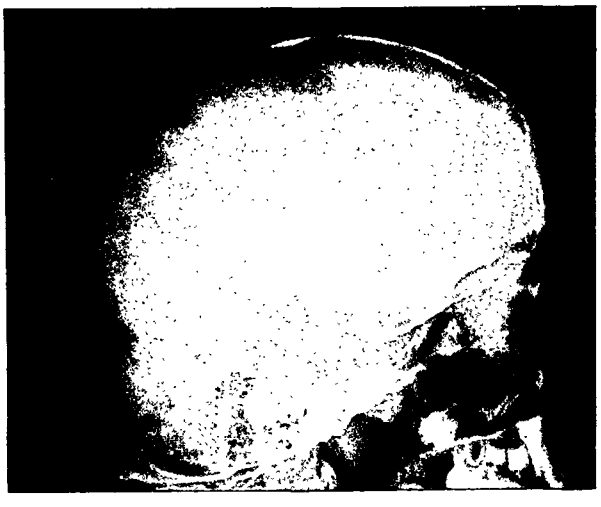


Fig. 3. Case 1. Roentgenogram of skull showing enlarged sella turcica.

is slightly greater than the average and the transverse diameter of the skull somewhat reduced as compared with the average. This gives a configuration somewhat suggestive of the dolicocephalic type of skull. The pituitary fossa is unusually deep. The convolutional markings on the inner table are slightly prominent. There is no unusual intracranial calcification and the mastoid and paranasal sinus development is relatively normal (Fig. 3).

Spine: Examination of the spine in both anteroposterior and lateral projections demonstrates a mild degree of scoliosis with the convexity of the curve to the right in the dorsal level. All of the bone structure is lacking slightly in mineral salt content. There is a spina bifida of the first and second segments of the sacrum (Fig. 4).

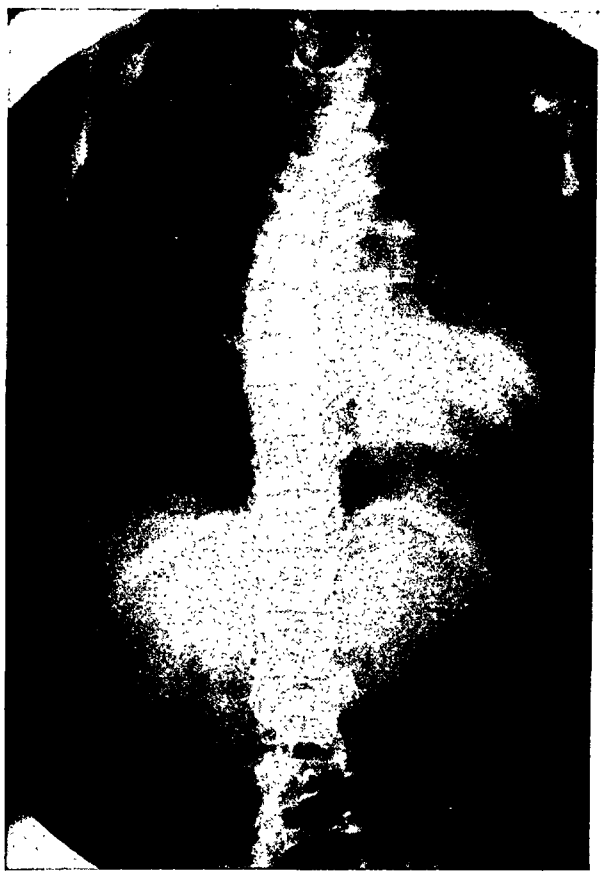


Fig. 4. Case 1. Roentgenogram of spine showing scoliosis.

Pelvis: No definite abnormality of the pelvis except for a minimal lack of mineral salt con-



Fig. 5. Case 1. Roentgenogram of pelvis. The exostosis or osteochondroma is seen in the right femur.

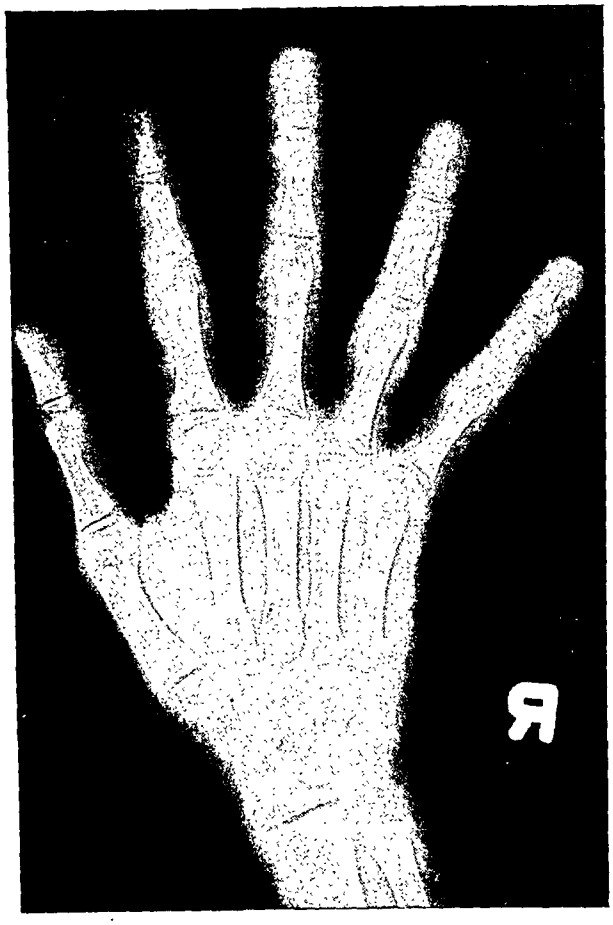


FIG. 6. Case 1. Roentgenogram of the right hand. There is demineralization of all the bones with elongation of the metacarpal bones and the phalanges of the digits.

tent of the bone structure. There is a suggestive osteochondroma on the inferior aspect of the lesser trochanter of the right femur (Fig. 5).

Hand: Film of the hand in the dorsopalmar projection demonstrates normal ossification of the bone structure, though all the bones are lacking in calcium content, and there is some elongation of the metacarpal bones and the phalanges of the digits. The entire configuration is that of arachnodactyly (Fig. 6).

Conclusions: All of the bone changes in skull, spine, pelvis and hand are rather characteristic of those seen in the so-called Marfan's syndrome, in which there is an associated arachnodactyly.

The keto-steroid output was 2.9 mg. in twenty-four hours which was high since a normal for this age is 1 mg.

The follicle stimulating hormone excretion for a twenty-four hour period was less than 7 mouse units which is normal for this age.

These studies were made, however, after the patient had been on methyl testosterone for approximately two months but none had been given a month previous to the keto-steroid and gonadotropin studies. (Contrast this with second case.) He was placed on 20 mg. of methyl testosterone on September 26 and by October 20 he had gained $3\frac{1}{2}$ lb. On November 1 he developed an acute cold and due to the fever and anorexia he lost $1\frac{1}{2}$ lb. However, by December 6, he weighed 40 lb. (18.1 kg.).

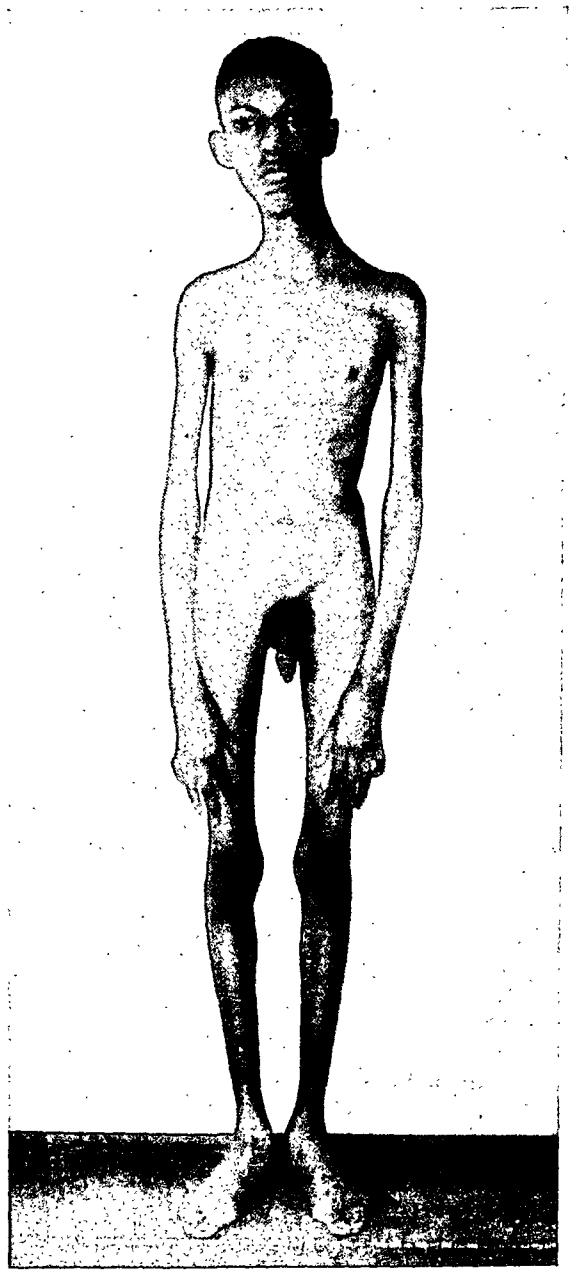


FIG. 7. Case II. Front view. The long arms are well shown, as is the asymmetry of neck, asthenic habitus.

Of importance are the changes noted in the span and height on this form of therapy: the span increased from 47 inches (119.3 cm.) on September 26, 1947 to 49 inches (124.46 cm.) on December 6, 1947, a gain of 2 inches (5 cm.). The height during this period of approximately two months increased from 46.5 inches (117 cm.) to 47.25 inches (119.8 cm.), a gain of $\frac{3}{4}$ inch (1.8 cm.).

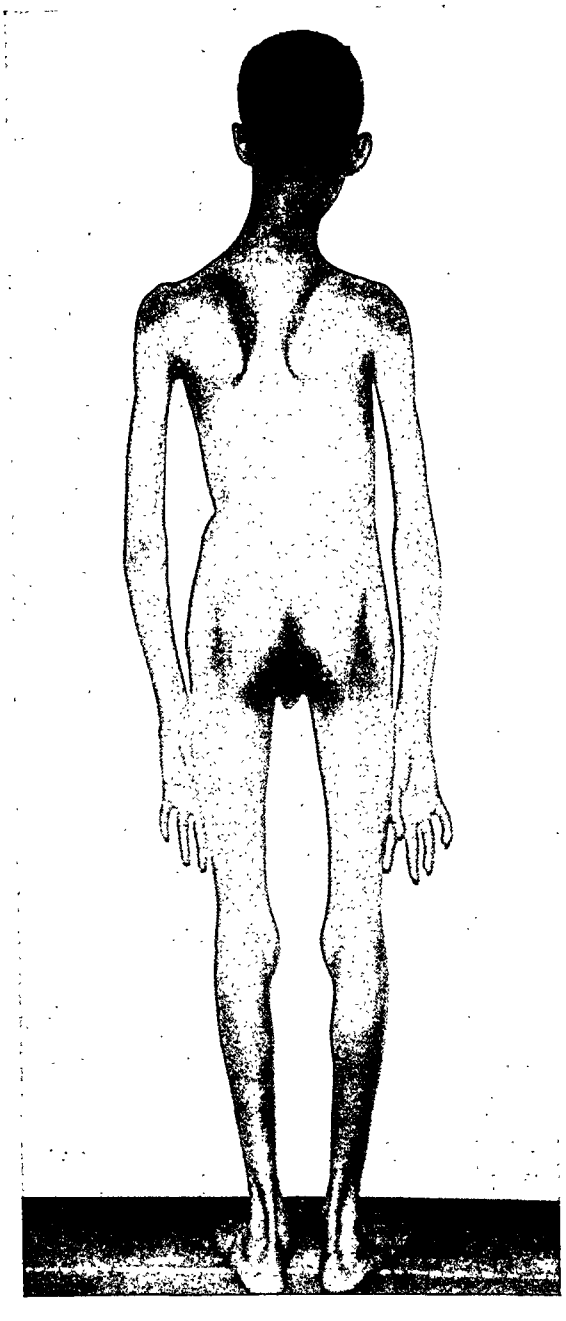


Fig. 8. Case II. Posterior view showing winged scapulae, spindly arms and legs.

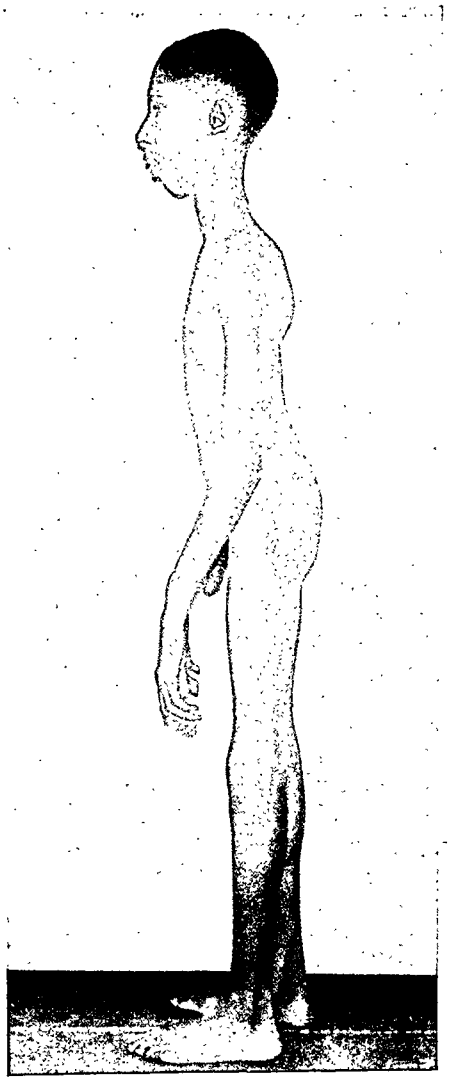


Fig. 9. Case II. Lateral view showing the general body build, and in an exaggerated degree the long spindly arms and legs. The recession of the lower jaw is well shown.

Case II. The patient was a fourteen year old colored boy. The history was not reliable since contact was through an "uncle." He had always been too thin and was always weak. He had previously been examined at Receiving Hospital and it was through the courtesy of the hospital staff and Mr. Arthur E. Parks,* a junior medical student, that this case is reported. Mr. Parks did the keto-steroid and gonadotropin studies on both cases. The "uncle" stated that the patient never looked "natural." Dizziness was complained of by the patient.

The physical examination showed a boy of

* From the Endocrine Laboratory of the Department of Research, Harper Hospital.



FIG. 10. Case 11. The high arched palate which is characteristic of cases of arachnodactyly.

asthenic build, undernourished, with the appearance of arachnodactyly (Fig. 7, 8 and 9). The skull was of the dolicocephalic type, the supraorbital ridges were prominent. There was no dislocation of the lens. The pupils were small but reacted normally. The auricles of the ears were large and protruding. The teeth were in fair condition with malocclusion and a recession of the lower jaw. The palate was of the high arched Gothic type (Fig. 10). The thyroid gland was small. The chest was deformed due to scoliosis. The scapulae were of the winged type. The scoliosis produced a marked asymmetry of the neck, chest and lumbar muscles. The heart was ptotic and a loud systolic murmur was heard all over the precordium with the loudest intensity over the aortic area. It was believed that a congenital cardiac anomaly was present but the type was not further determined. The pulse rate was 84, and the blood pressure was systolic 106 mm., diastolic 80 mm. The limbs, hands and feet were long and slender showing the characteristic spider-like extremities. The skeletal muscular system was poorly developed and hyperextensibility of the joints was present associated with apparently poor development of the ligamentous tissues. There was subluxation of the ankle joints. Absence of the subcutaneous fat was everywhere apparent. The genitalia were well developed. The arms were long, reaching almost to the knees. The measurements were as follows:

	PATIENT		NORMAL	
	inches	cm.	inches	cm.
Head	21.25	(54)	21.6	(55)
Chest	25.5	(65)	29.1	(84)
Waist	23.0	(58.42)	25.4	(64)
Span	66.25	(168)	62.1	(158)
Upper	32.25	(82)	29.9	(76)
Lower	31.25	(79)	30.8	(78)
Height	63.5	(161) lying down	60.7	(154)
Weight	61.75	(28 kg.)	92.9 lb.	(42 kg.)

The height was 61.25 inches (155 cm.) when standing due to the scoliosis which therefore reduced the height (Fig. 8). The roentgenograms were reported as follows:

Lateral Skull: The tables of the calvaria are of average thickness and there is no evidence of increased intracranial pressure and there is no unusual intracranial calcification. No demonstrable abnormality of bony development in the facial area. The sella turcica is shallow (Fig. 11).

Single Chest: No roentgen evidence of cardiovascular or pulmonary disease. There is noted, however, a moderate degree of scoliosis with the

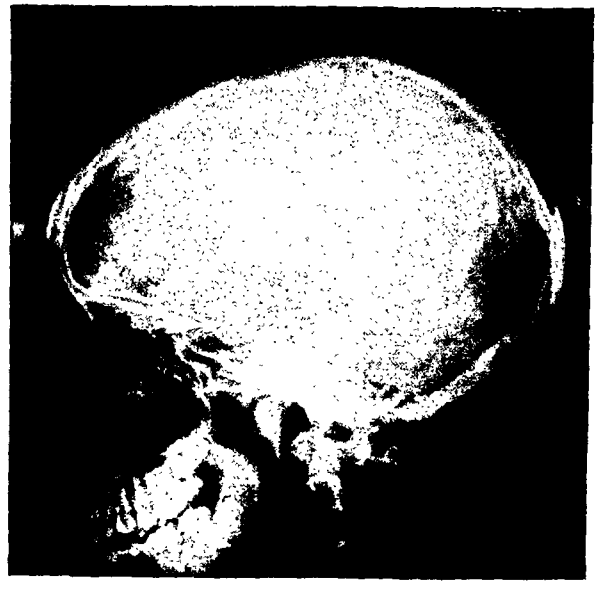


FIG. 11. Case 11. Lateral roentgenogram of the skull.

convexity in the lower dorsal level toward the right side (Fig. 12).

Both Hands: The bones of the digits and also the metacarpal bones are unusually long and the entire picture is suggestive of arachnodactylia (Fig. 13). The roentgenograms of the spine were reported as follows:

Lateral Spine: Segments of the spine, as seen in the lateral projection, are straight, there being loss of the normal lordotic curve in the lumbar level and a mild kyphosis is present in the dorsal level.

The laboratory studies made at Receiving Hospital were reported as follows:

Urinalysis: negative.

Glucose tolerance test:

Fasting 46 mg.
1 hour 111 mg.
2 hours 79 mg.
3 hours clotted.
4 hours 57 mg.
5 hours 32 mg.
6 hours 41 mg.

All urines negative for sugar.

Kepler water test: night specimen 26 cc. Largest day specimen 70 cc.

Blood urea: 34 mg.

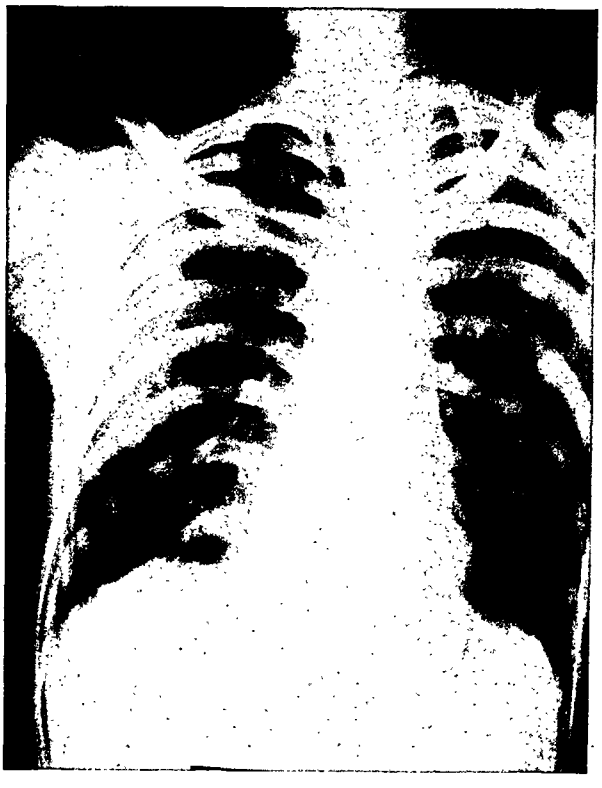


Fig. 12. Case 11. Chest roentgenogram showing scoliosis of spine. The heart size was considered normal.

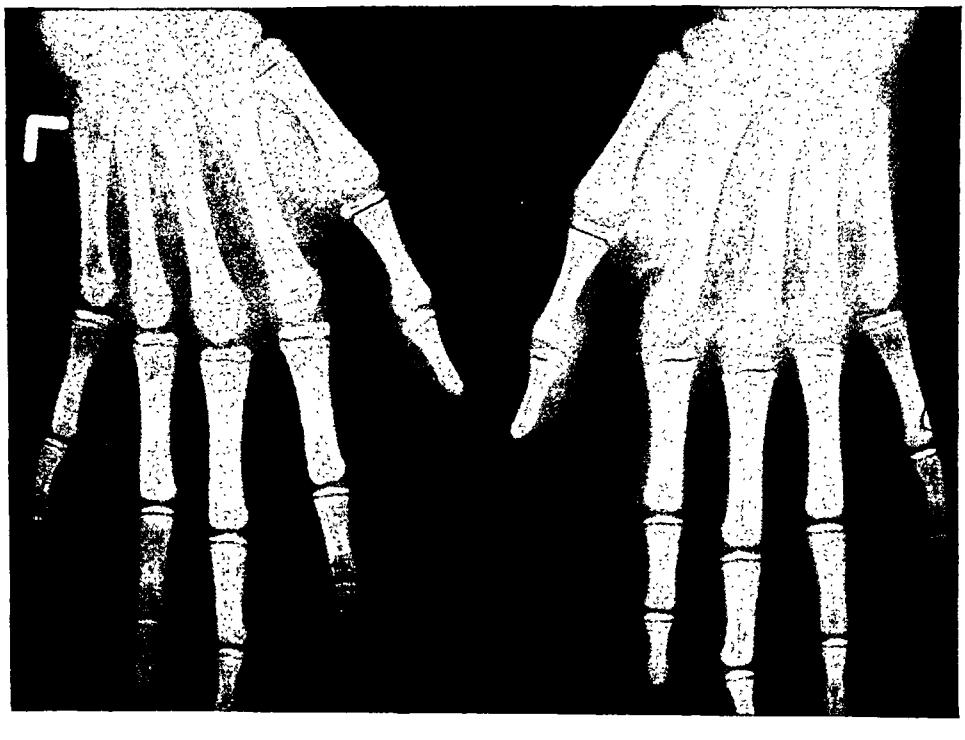


Fig. 13. Case 11. Roentgenograms of hands showing unusual length of digits and metacarpal bones.

Blood creatinine: 0.9 mg.
Kline reaction negative.
Kahn reaction negative.
Blood count: Red cells 4.7 million. Leukocytes 9,050, with a differential count of 61 per cent polymorphonuclears, 33 per cent lymphocytes, 4 per cent monocytes, 2 per cent eosinophils; hemoglobin 14 grams.
The visual fields were normal. No lens abnormality.
The follicle-stimulating hormone excretion was reported as 26 mouse units in twenty-four hours. The 17-keto-steroids were reported as 4.1 mg. per twenty-four hours. These values are normal for a fourteen year old boy.

COMMENT

In arachnodactyly the congenital defects are evident and certain data to be presented indicate that we are dealing with a primary pituitary defect which results in the target tissues, particularly the mesoderm, being defectively developed. Weve[13] called attention to the defect in the development of the mesoderm. Objection to this opinion is based on the fact that some of the typical ocular findings are in the ectodermal structures such as the lens and muscle of the iris. However, as we know, the supportive tissues in general and specifically in the eye, the vascular system, are mesodermal in origin and the lens and iris-muscle depend for their support on this layer. Weve concluded that the syndrome is a congenital inherited entity which produces a mesodermal dystrophy. Concerning its etiology he said that all we know is that it is mostly an inherited condition. He was of the opinion that the eye weakness could be explained by primary mesodermal disturbances. The whole mesodermal layer partakes of the underdevelopment as shown by the aforementioned eye changes, the small slender bony structures with kyphoscoliosis, lax ligaments, small muscles, secondary anemia (mesodermal blood) small kidneys, small genitalia, lack of subcutaneous fat, poorly developed vascular system and dissecting aneurysms. Of importance is the underdevelopment and defect of the cardiovascular system which may be due to a primary pituitary disturbance.*

The high arched palate present in the 2 cases reported by Tobin and his associates as well as the high arched palate in the 2 cases herein reported and in both parents of the first case place this finding in a highly important etiological position.

This clinical finding of a high arched palate in each of 21 cases of retinitis pigmentosa was reported by Pino and me[7] and was subsequently verified by Givner and Bruger.[4] Gadbaw and I[6] gave further data concerning the significance of this finding. It was thought that the high arched palate indicated a pituitary disturbance and was related to the development of the pituitary and may be the result of abnormal embryological development of this gland. Most cases of arachnodactyly have a dolicocephalic head associated with a high arched palate. Mortimer[8] studied 494 cases of cranial dysplasia in human beings and concluded that 60 per cent of the patients who showed evidence of disturbance in cranial form and structure, presumably during the growth period, suffered subsequently at some time or another from a dyspituitarism that was recognized physiologically. As is known the pituitary develops from the roof of the mouth and there seems to be no question that the high arched palate and embryological development and function of the pituitary are etiologically related. Stockard and Johnson[10] in their studies on dogs with crossbreeding of various species found that: "The one character common to all breeds and hybrids in which structural misfits occur is an abnormality of the pituitary gland. Such an array of growth disharmonies in association with pituitary abnormality makes it seem highly probable that the pituitary secretions are largely concerned with the normal regulation and adjustment of growth among the organ systems and bodily parts. It should be remembered that many of these disharmonious arrangements are strictly inherited

* Work is now in progress in association with Dr. Louis Jaffe on the pituitary-vascular relationship.

in very definite fashion. This fact may mean that the related peculiarity of the pituitary is the primarily inherited character, while the structural derangements are secondary results due to the failure in harmonious growth regulation by the genetically modified pituitary gland." This would indicate that the pituitary gland is the primary factor in the development of the high arched palate. Most authors agree that the pituitary is the endocrine gland most frequently involved in arachnodactyly.

Tobin and his associates stated that the possible role of the endocrine glands in Marfan's syndrome has been debated repeatedly. There is no anatomic evidence, according to these authors, to implicate any of them but the pituitary. These changes are in the nature of an eosinophil hyperplasia. A deep sella was seen in the first case, and a hypopituitary type of glucose tolerance curve was seen in the second case. The curve was like that seen in hypophysectomized animals and in pituitary cachexia of humans.

The evidence points in the direction of a pituitary involvement. What is of interest is the finding of an eosinophil hyperplasia in several of the autopsied cases of arachnodactyly. This finding is usually associated with overgrowth of tissues, such as in acromegaly and gigantism. Despite the eosinophil hyperplasia the clinical picture is unmistakably that of pituitary underactivity. Support for the opinion that eosinophil hyperplasia may be associated with pituitary hypofunction is found in mongolism. Benda's work[2] on mongolism helps to understand the eosinophil hyperplasia. His conclusions on this phase of mongolism are as follows:

> A study of the pituitary in mongolism reveals pathology which indicates that this condition is associated with abnormal pituitary function. In contrast to cretinism in which the pituitary tends to be enlarged the pituitary in mongolism is hypoplastic. Abnormally low secretory activity is indicated by (1) inability to produce secretory cells and granules and (2) by abnormal granule storage (stagnation) and disappearance of signs of secretory activity. In the first group, there is evidence of hypopituitarism with absence of these granule types which we have seen to be connected with all secretory activity. The gland fails to produce and store potent agents. In the second group the secretory elements are filled with one type of granule (alpha granules) while the beta cells regress to castration cells or delta cells (large chromophobes). The secretory chief cells (gamma cells) are underdeveloped. Mongolism is the congenital type of hypopituitarism.

That the clinical picture is one of hypopituitarism is evident and that the pituitary cells can respond is shown by the growth induced by testosterone as represented in the first case.

In epilepsy, migraine, and retinitis pigmentosa a high arched palate is common and, as noted, also in arachnodactyly. And like the latter disease the aforementioned diseases are associated with congenital defects such as hammer toes, spina bifida occulta, spinal deformities, cervical ribs and others.

Ulrich[12] studied 500 cases of migraine, and recorded the occurrence of a general disharmony in bodily development: premature graying of the hair, abnormal growth and distribution of hair, confluent eyebrows, convergent or divergent strabismus, asymmetric distribution of the pigment in the iris, myelinated nerve fibers in the retina, color blindness, irregular and abnormal development of the forehead, supernumerary nipples, small or undescended testicles, microcephaly with normal intelligence, cervical ribs and inequality of the breasts.

The fact that migraine, epilepsy, retinitis pigmentosa and arachnodactyly have a common denominator in the form of a high arched palate and malformations in bodily development indicates that there may be a common etiological factor. The embryological development of the hard palate, the pituitary gland, the hypothalamus and the optic system, also points to a common etiological factor in the produc-

tion of these diseases; at least speculation has been centered in these areas in a search for their etiology.

Duoparental inheritance factors in the case likewise point in the direction of the pituitary-hypothalamic area as the etiological factor. The fact that there were high arched palates in the patient and the parents, as well as shortness of stature in the asthenic type mother, diabetes mellitus in the maternal grandmother, epilepsy in a paternal cousin adds some force to the opinion that the pituitary was a prime factor in the production of arachnodactyly. It has been shown that the pituitary has a selective action on the mesodermal layer of the body. The accumulated data indicate that a defective pituitary will result in symptoms mainly found in the mesoderm. This would indicate that in arachnodactyly there is a congenital inherited pituitary-mesodermal defect.

The second case was in a Negro and this race has a peculiarity of the mesoderm. Several years ago I[5] showed that the mesoderm of the Negro was unique in many respects when compared with that of the white race. The Negro race's relative immunity to ectodermal, epithelial and nervous system disturbance was also emphasized.

A few examples of the unique character of the Negro's mesoderm are as follows:

It is a generally accepted fact that the Negro has a tendency to connective tissue overgrowth which predisposes him to keloids, fibroids, strictures, neurofibromatosis, and other connective tissue disturbances. The mesodermal hemopoietic system has a singular character in that sickle cell anemia is practically limited to this race. Furthermore pernicious anemia, thromobocytic purpura, and leukemia, are not common in the pure Negro.

The mesodermal blood vessels are attacked with undue frequency resulting in aneurysms (syphilitic and non-syphilitic), arteriosclerosis, and vascular disease in general. The lymphatic, osseous, and cartilaginous systems also show a predisposition to disease in the Negro. That the Negro also suffers not infrequently from arachnodactyly is shown by the report of cases by Futcher and Southworth;[3] Rambar and Denenholz,[9] and Baer, Taussig and Oppenheimer.[1]

The osseous system has certain similarities to eunuchoidism in which the extremities are long and slender and the epiphyses remain open for an abnormally long period. In the first case the span was 3 inches (7.5 cm.) greater than normal and the height $1\frac{1}{2}$ inches (3.75 cm.). Within a period of approximately two months on a daily dose of methyl testosterone the height increased $\frac{3}{4}$ inch (1.8 cm.) and the span increased 2 inches (5. cm.).

In the second case the span was also approximately 4 inches (10 cm.) greater than normal and the height 3 inches (7.5 cm.) more than normal. Tobin's first case had grown 24 inches (61 cm.) in seven years, reaching a height at twenty years of 79 inches (200 cm.).

In the first case the mother was 61 inches (155 cm.) in height and weight 98 lb. (44.5 kg.), indicating an asthenic mesodermally weak individual. The maternal grandmother had diabetes mellitus, a disease in which the pituitary also plays a role. A paternal cousin had epilepsy.

SUMMARY

Two cases of arachnodactyly are reported. The first case was a six year old boy with subluxation of the lens and tremulousness of the iris (iridonesis). A congenital cardiac defect was assumed to be present. A large sella turcica was present. A response in height and weight to methyl testosterone took place within a period of two months. An increase in the output of 17-keto-steroids followed this therapy. The follicle-stimulating hormone output in both cases was normal.

The second case was in a fourteen year old Negro boy with no dislocation of the lens, a possible congenital cardiac defect, a marked increase in glucose tolerance; the curve was actually hypoglycemic like that

seen in pituitary cachexia or severe hypopituitarism.

A high arched palate was present in both cases and in the parents of the first case. This finding seems to be characteristic of arachnodactyly, and its significance in this disease as well as in migraine, epilepsy and retinitis pigmentosa associated with disharmonious bodily development was discussed. It was assumed to be related to the development of the pituitary, the anterior lobe of which originates embryologically from the roof of the mouth. This gland is probably an etiological factor in the production of arachnodactyly. The etiology may rest in a primary inherited pituitary disturbance and a secondary mesodermal tissue defect. The opinion that arachnodactyly is an inherited mesodermal defect is supported.

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THE QUANTITATIVE EVALUATION OF BONE DENSITY

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IN THE past the most common method for the appraisal of bone density and mineralization from roentgenograms has been by the subjective impressions of the roentgenologist or the research worker. An attempt was made by the senior author in 1927, and by Stein[8] and by Sanders[6] in 1937 to reduce skeletal mineral density evaluations to a somewhat objective basis through the use of a stationary beam of light passing through a certain area of a bone roentgenogram, also stationary, onto a photronic cell. The use of a static technique of this character, however, is attended by large variations, because the same anatomical position in the skeletal roentgenogram of the bone of different animals or human subjects, or of the same subject at different times cannot be located accurately by a stationary beam of light shining through a non-moving film.

In 1929 the senior author adapted a photographic tracing densitometer, built in the Department of Physics at The Pennsylvania State College for scanning spectrum photographs, to the problem of obtaining tracings of skeletal roentgenograms. At first, roentgenograms of the rat femur were traced, and later various bones of human subjects were evaluated by means of this instrument. Although a poor degree of reproducibility was obtained with this original instrument, particularly with any but large bones—because it lacked the refinements needed for precise results—its use demonstrated that the principle of making tracings from one landmark to another by means of a stationary beam of light and a moving film eliminated the basic difficulty with the static technique; namely, that of failing to locate the same area of the same bone roentgenogram twice in succession, or a comparable area in films of two or more bones.

In 1936, means became available to the senior author to procure a Type B Moll Recording Microphotometer from Holland; the instrument was designed for making tracings of spectral lines on photographic plates. A thermocouple served as the light-sensitive part of the apparatus, and this showed very slow response to changes of density as the film traveled through the beam of light. Other features of the instrument rendered it unfit in its original condition for the purpose of tracing roentgenograms of human beings and experimental animals. Through the technical assistance of Ernest Axman and of Warren Mack, the instrument was modified by the substitution of a photronic cell, and in many other respects. After two and one-half years of successful use of this device with roentgenograms of human subjects, Mack, O'Brien, Smith and Bauman[4] described the method as then developed.

From 1942 to 1949 the microphotometer and the general method of its use have undergone numerous further refinements, which have increased the precision and widened the range of bones which could be evaluated quantitatively; the method now is applicable to anything from the mouse femur to the skull of man, within a very small limit of error.

The accuracy of the microphotometric scanning procedure for evaluating the mineral density of animal and human bones depends upon the validity of two assumptions:

(a) *that the photographic density of the image on a roentgenogram is related in a known manner to the density of*

* Deceased October 20, 1945.

the mineral of the bone upon which the roentgenogram is based; and

(b) *that, through the use of a step wedge or ladder made of a substance of homogeneous density and generally similar in chemical composition to bone, placed on the film at the time when the exposure is made, corrections can be applied for unavoidable variations in exposure and development technique, within satisfactory limits.*

Quantitative measurements have been made on several thousand roentgenograms derived from living and cadaver bones of human and animal origin. In the Pennsylvania State College mass studies in human nutrition, conducted in the Ellen H. Richards Institute since 1935, the os calcis, the anteroposterior aspect of the foot, the hand, the elbow, and the knee are roentgenographed routinely. In certain longitudinal studies under the same auspices, the hip, the femur, the patella, the shoulder, and the skull are added to the routine series. From an evaluation of the foregoing, these conclusions may be drawn:

(a) The measurement of density of bone mineral by specially prepared roentgenograms can be accomplished with an error of only a few per cent. The method has a sound theoretical basis.

(b) Living bones act somewhat as reservoirs of calcium salts and take on or give up calcium compounds in accordance with the nutritional status of the individual, and other factors.

(c) Certain parts of certain bones react very quickly (within a few days) to changes in nutritional status, while other bone regions make relatively slow changes.

(d) Measurement of bone density in this way appears to have considerable promise as a clinical tool for determining the calcium nutritional status of an individual relative to the norm, and for detecting changes in calcium nutritional status caused by pregnancy, illness, change in diet, or other causes.

(e) The technique appears to offer significant advantages in medical research experimentation with mice, rats, and other animals, where it now is necessary to evaluate changes in skeletal status with time by killing part of the group periodically in order to make a chemical analysis of the bones. The present technique is suitable for bones even as small as those of mice, and would greatly reduce the number of test animals required in this type of work.

Preliminary to a discussion of the experimental technique, an outline of the pertinent theoretical considerations will be presented.

THEORETICAL CONSIDERATIONS

Roentgen-Ray Absorption. As is well known, roentgen radiation is absorbed in accordance with the relationships.

$$I = I_0 e^{-\mu x}, \tag{1}$$

where I_0 is the intensity of the beam of radiation striking the object, I is the intensity of the beam at some point located at a distance, x, inside the object, e is 2.718 . . . , the base of the system of natural logarithms, and μ is a quantity commonly referred to as the roentgen-ray absorption coefficient (linear).

The differential equation from which equation (1) is derived is:

$$\frac{dI}{Idx} = -\mu, \tag{2}$$

where it can be seen that μ also equals the fractional part of the intensity absorbed while the beam traverses a small distance, dx. Since the absorption results from the presence of atoms of an absorbing element in the path of the beam, the number of atoms encountered by the beam in a distance, dx, will be denoted by dn. Then, equations (1) and (2) can be written in another familiar form, in terms of n, the

number of atoms penetrated and μ_a, the atomic roentgen-ray absorption coefficient, as follows:

$$I = I_0 e^{-\mu_a n} \tag{1a}$$

$$\frac{dI}{Idn} = -\mu_a \tag{2a}$$

μ_a is equal to the fractional part ot the energy absorbed on the average by one atom. In addition, a mass roentgen-ray absorption coefficient, associated with the absorption per unit mass of a particular substance, frequently is used. For the following discussion, it is most convenient to work with the atomic absorption coefficient, μ_a.

The Role of Scattering. Roentgen-ray absorption coefficients for most elements and wavelengths have been determined experimentally and are published in reference books. Several empirical formulas have been developed to express the absorption coefficient, in terms of the atomic number (Z) of the absorbing element, and the wavelength (λ) of the radiation. These expressions are of the form:

$$\mu_a = AZ + BZ^4\lambda^3. \tag{3}$$

The first term is the "scattering" term and the second term is known as the "fluorescent" or "true" absorption term. As the word "scattering" suggests, the first term in the absorption coefficient according to the classical definition does not represent absorption in the strictest sense of the word, but refers merely to a redirection or scattering of the radiation without important changes in the wavelength or energy. The second term represents true absorption of energy by the atoms involved.

The reason for including scattering in the classical definition of absorption can be seen from a consideration of the experimental apparatus used to measure the absorption coefficient. As indicated in Figure 1, a very sharp, pencil-like beam consisting essentially of monochromatic radiation is produced by the use of a filter and narrow slits; this is allowed to strike the specimen of which the absorption coefficient is to be determined. On the opposite side of the specimen there is placed a second series of slits, arranged colinearly with the first set of slits, together with a radiation detector. The ratio of I to I_0 is determined by comparing the detector readings with the specimen in place, and again not in place. The absorption coefficient then is computed from equation (1) or (1a). Only a very small amount of the total scattered radiation reaches the detector because of the slit system. This experimental procedure for measuring the absorption coefficient leads to the accepted value wherein the radiation scattered by the specimen and

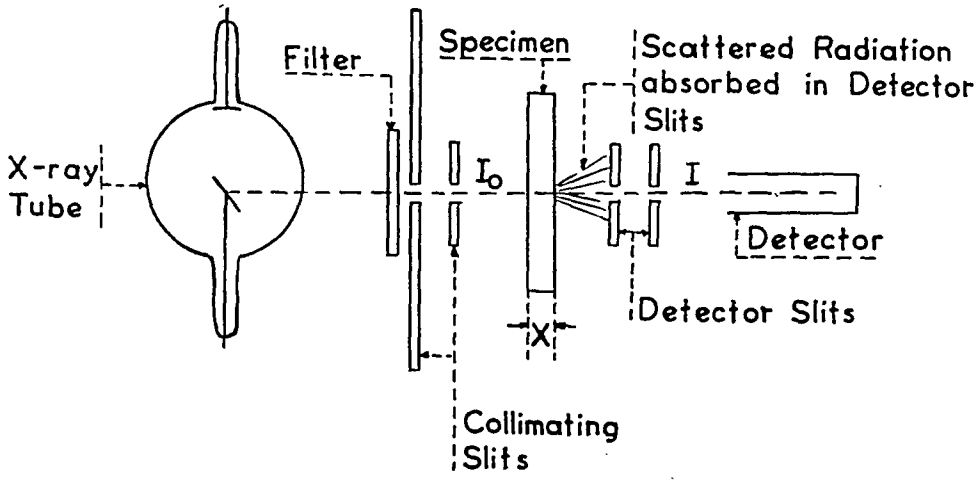


FIG. 1. Apparatus for measuring roentgen-ray absorption coefficient.

absorbed by the slits is considered to have been absorbed by the specimen. The procedure is most expedient because of the difficulty of collecting at a detector all or any known fraction of the scattered radiation.

When a roentgenogram of an object, such as a bone, is made, the radiation scattered from the various parts of the object is not absorbed by narrow slits, and a substantial part thereof falls onto the bone image, thus increasing its photographic density. The energy scattered from any particular portion of the bone is radiated in all directions, and the effect of the scattering is a general fogging or relatively uniform blackening of the film. The intensity of the roentgen radiation striking the film at any point on the bone image thus is greater than that which would be given by equation (1); and conversely, the thickness of the object, as calculated from measured values of I/I_0 and tabulated values of the absorption coefficient would be smaller than the actual thickness.

The scattering difficulty can be reduced in theory, and to a considerable extent in practice, by using radiation of a relatively long wavelength, or lower kilovoltage, so that the second term of equation (3), which is proportional to the third power of the wavelength, is very large in comparison with the scattering term, which is independent of the wavelength. A practical limitation arises from the higher radiation intensities and exposure time required for object penetration with low kilovoltage radiation. The scattering consideration may be of less importance where the absorbing specimen is composed of a chemical element having a high atomic number; but for such a specimen the practical necessity for using shorter roentgen-ray wavelengths to secure sufficient penetration may offset the discrimination against scattering afforded by the higher atomic number. As will be shown later, the technique under discussion includes an approximate correction for the effect of scattered radiation.

Comparison of Possible Techniques. At first glance, it might appear that measurement of roentgen-ray absorbing power for the purpose of determining the mineral density of living bones is not feasible. Bones are not uniform in density and have an irregular three-dimensional shape, with the result that measurements of mineral density on particular sample points of the bone cannot be reproducible or reliable as stated earlier. Instead, the present technique involves a measurement of the mineral density averaged over an entire bone cross-sectional area for which a microphotometric tracing of the roentgenogram is made. The averaging procedure which takes place automatically when a trace is made between defined landmarks on the bone image by a stationary beam of light through a moving film disposes of the reproducibility difficulty inherent in the stationary beam—stationary film technique. In the latter, the relative positioning of the roentgen tube, the bone, and film, together with the location of the light spot on the bone image cannot be controlled with sufficient accuracy to insure that the mineral density at specified penetration positions in different bones or in the same bone at different times can be compared with any reasonable significnce.

In order to determine the mineral density from the number of atoms which the roentgen-ray beam has penetrated, it is necessary to measure I/I_0 for substitution into equation (1a). There are three general types of apparatus available for the detection and measurement of roentgen radiation. These are the ionization chamber, the fluorescent screen, and the photographic plate or film. Although the ionization chamber is conceded to be the most suitable device for the quantitative measurement of roentgen-ray intensity, it presents considerable experimental difficulties if one desires to obtain the average absorption of a considerable portion of bone; in the latter case, the bone to be measured would have to be placed successively in a large number of different and accurately controlled positions relative to the roentgen-ray beam going from the

tube into the ionization chamber, and it would be necessary to record the ionization chamber current for each of these positions. In addition to the difficulty of acquiring such data with living human or animal subjects, this method does not provide as complete and detailed a permanent record as would be desired.

The second device, the fluorescent screen, does little more than make an instantaneous conversion of the roentgen-ray

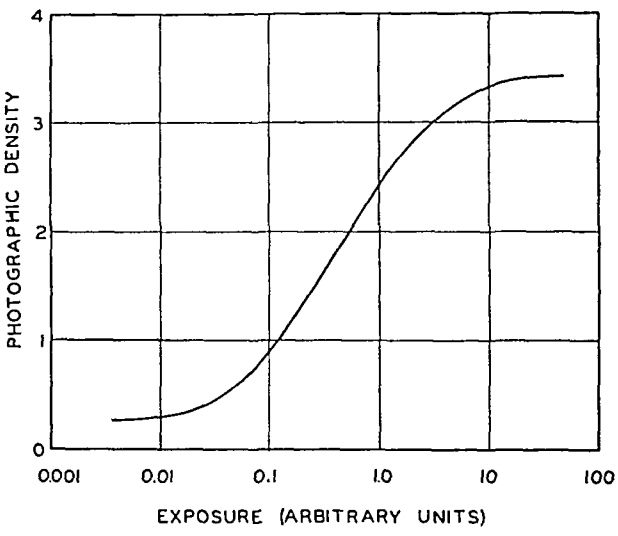


FIG. 2. A typical Hurter and Driffield (H and D) characteristic for photographic film.

image into a corresponding image of visible light, This visible image, if produced in a darkened room, could be scanned with a photoelectric device, and essentially the same data could be derived therefrom as with the ionization chamber method. Another variation would consist of photographing the fluorescent screen and evaluating the photograph at leisure. Use of the fluorescent screen in this way offers the possibility of simultaneous visual observation and permanent photographic recording of the data, although detail in bone density might be sacrificed to a certain extent by this technique.

The third detecting device, roentgen film, is known to possess certain characteristics not suited to a quantitative measurement of stimuli, without the application of special techniques. The roentgenographic technique is well understood and widely used in the medical profession, however, and offers the additional advantage of providing a detailed and permanent record of the bone. The direct roentgenogram resembles the photograph which might be taken of the roentgen-ray energized fluorescent screen. All of the experimental work in connection with the present technique has been carried out by direct roentgen-ray exposure of the bone image on standard non-screen roentgen film, and the following discussion will relate primarily to this particular method, although in many instances the analysis will be directly applicable to the other possible methods mentioned above.

Analysis of a Technique Using Roentgen Film. A technique in which the blackening of a photographic plate or film is to be used as a quantitative measure of exposure requires the establishment of some procedure for determining the sensitometric curve of the plate or film, also known as the Hurter and Driffield Characteristic. This relationship varies so greatly with development and exposure conditions and with the particular emulsion that it has been found necessary to make a separate determination of the sensitometric curve for each film used to measure exposure values quantitatively. The curve of photographic density or blackening versus exposure is of the general shape of the Hurter and Driffield (H and D) curve shown in Figure 2; the nearly horizontal position of the curve occurring at low density levels corresponds to the situation in which the density approximates that of the unexposed film base, and the exposure is not sufficiently great to exercise appreciable effect upon the emulsion. The nearly horizontal portion of the curve occurring at a high density value is associated with exposures sufficiently long to expose the emulsion so completely that further increases in exposure cause little increase in density.

It is important, in using film to measure intensity or exposure, to keep the exposures on the comparatively straight central portion of the Hurter and Driffield curve, in

order that a small variation in exposure will show up as a measurable change in photographic density. If the range of exposure is very small, it often is sufficient to consider the curve to be a straight line. In the latter case, determination of the slope of the curve at the midpoint of the exposure range may suffice for measurement of exposure ratios. Most roentgenograms of bones, however, involve a wide range of exposure. Hence, it becomes necessary to construct a major portion of the sensitometric curve in order to make measurements of exposures. As will become apparent, the operation of correcting for the sensitometric curve can be combined with several other correction operations with an economy of labor and complexity.

Equation (1a) can be written also in the form:

$$n = \frac{1}{\mu_a} \ln_e \left(\frac{I_0}{I}\right), \tag{4}$$

where n represents, as before, the number of atoms in the path of the beam. If the continuous spectrum roentgen radiation generated by standard medical equipment is employed, I_0 and I will involve radiation of many different wavelengths, λ, for each of which a different μ_a value, as given approximately by equation (3), will apply. In fact, as the continuous or white radiation penetrates an object, its spectrum shape changes considerably because the softer or longer wavelength roentgen rays in the spectrum undergo more absorption, as is indicated by equation (3). As a result, the overall rate of absorption becomes greatest near the exposed surface where there is a large proportion of long wavelength radiation in the beam, and diminishes as the radiation penetrates farther into the absorbing object. In addition, if the average density of the bone is to be evaluated, procedure must be found to take into account the general non-uniformity of bone density, which causes $\rho(x)$, the atomic density, or number of absorbing atoms per cubic centimeter of bone to vary with the distance of roentgen-ray penetration. Fortunately, these difficulties can be resolved by the following procedure, which allows quantitative determination of bone density from roentgenograms prepared with standard continuous spectrum roentgen-ray machines of the type commonly used in medical work.

Let the bone of which the density is to be determined be exposed on the roentgen film, and at the same time let there be exposed for reference purposes a wedge-shaped object of known dimensions and chemical composition. Figure 3 shows a cross sectional view of the roentgen tube, the bone, the wedge, and the roentgen film. The position of the cross section is defined by the tracing path on the film and the focal spot of the roentgen tube.

For the time being it is assumed that the roentgen rays are monochromatic or of single wavelength, and that the bone and wedge both are comprised of a single absorbing element. It is assumed, also, that the roentgen tube is sufficiently far from the absorbing objects that the wave front essentially represents a plane. Referring now to equation (4), I_0 is taken to be the intensity of the radiation incident upon the top of the bone and wedge, and I is taken to be the intensity of the beam emergent from the bone or wedge and striking the roentgen film. Moreover, n represents the total number of absorbing atoms encountered by the roentgen-ray beam in passing through the bone or wedge. Referring again to Figure 3, $f_1(x)$ and $g_1(x)$, respectively, represent the top boundary curves of the bone and wedge, and $f_2(x)$ and $g_2(x)$ denote the corresponding bottom boundary curves. For convenience, the length of the roentgen-ray path through the bone cross section is represented by $F(x) = f_1(x) - f_2(x)$ and the length of the radiation path through the wedge by $G(x) = g_1(x) - g_2(x)$. The density of the bone cross section, expressed in atoms of absorbing element per cubic centimeter, is denoted by $\rho(x,y)$; note that this quantity depends both upon the x and upon the y coordinates of the point on the bone cross section at which it

is evaluated. The wedge is assumed to be perfectly uniform in atomic density, which is denoted by ρ'.

From the definition of n, for the bone image at the point, x,

$$(5) \qquad n(x)=\int_{f_2(x)}^{f_1(x)}\rho(x,y)dy=\bar{\rho}(x)F(x),$$

and for the point x' on the wedge image,

$$(6) \qquad n'(x')=\rho' G(x).$$

The notation, $\bar{\rho}\,(x)$, denotes the average tracing path a point, x', on the wedge image having the same blackness or density can be found, then, for these corresponding points,

$$(9) \qquad I(x)=I'(x'), \quad \text{and}$$

$$(10) \qquad \mu_a\bar{\rho}(x)F(x)=\mu_a'\rho' G(x')$$

$$(11) \qquad \bar{\rho}(x)=\frac{\mu_a' G(x')}{\mu_a F(x)}\rho'.$$

Equation (11) states that the atomic density of the bone, averaged along the

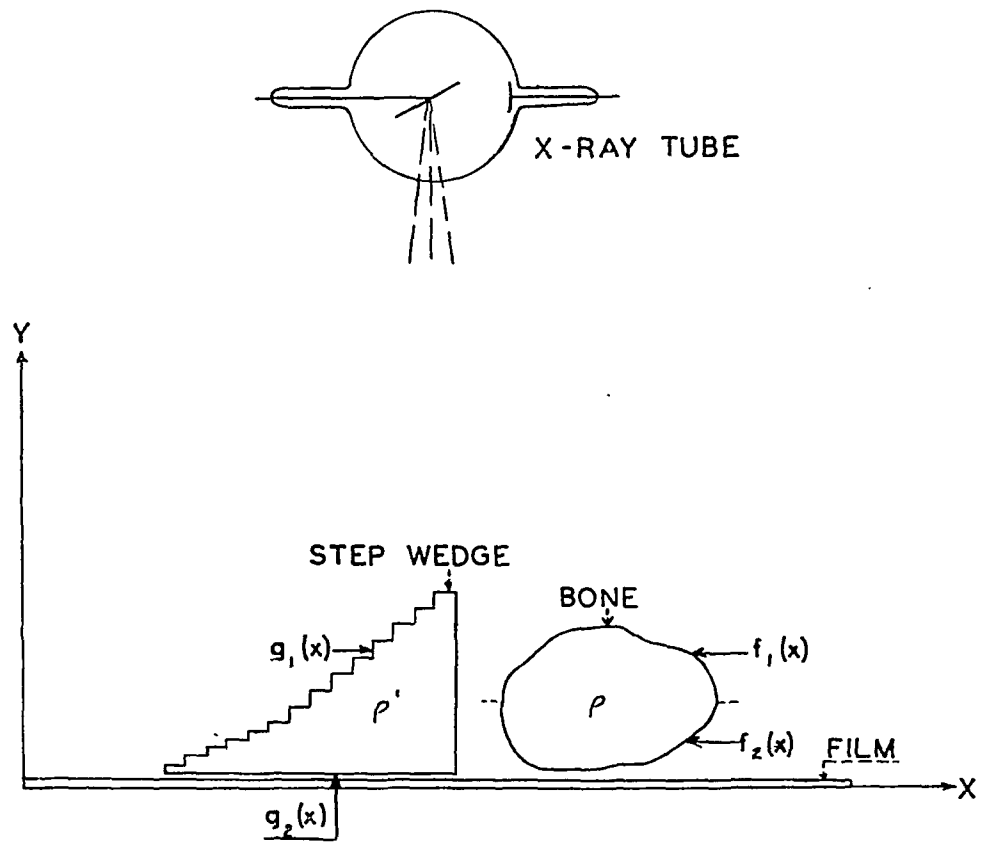


FIG. 3. Schematic diagram of roentgen tube, wedge, bone and film.

atomic density along the roentgen-ray path.

From equation (1a) the roentgen-ray intensity incident on the film under the bone at the point, x, is

$$(7) \qquad I(x)=I_0e^{-\mu_a n(x)}=I_0e^{-\mu_a\bar{\rho}(x)F(x)},$$

and under the wedge at the point, x', is

$$(8) \qquad I'(x')=I_0e^{-\mu_a n'(x')}=I_0e^{-\mu_a'\rho' G(x')}.$$

If for any point, x, on the bone image path of the roentgen-ray beam, equals the corresponding atomic density for the wedge, multiplied by the ratio of the absorption coefficient of the wedge atoms to the absorption coefficient of the bone atoms, and also multiplied by the ratio of the path length in the wedge corresponding to the point x' to that in the bone for the point, x.

Up to this point in the discussion, it has been assumed that the illuminating roent-

gen rays are monochromatic and that there is only a single absorbing element both in the wedge and in the bone. Equation (11) is subject to these two limitations, which will be considered next.

If the illuminating roentgen radiation is of the continuous spectrum type, validity of the above analysis requires that $I(x)=I'(x')$ for every wavelength in the spectrum. Because the sensitivity of emulsions varies with wavelength, points of equal photographic density on the two images do not necessarily arise from equal roentgen radiation intensity unless the spectral distribution is the same for the two points. Consequently, the expression, $\frac{\mu_a'G(x')}{\mu_aF(x)}$ must have the same value for all wavelengths in the spectrum. $\frac{G(x')}{F(x)}$ is determined only by the physical dimensions of the absorbing objects and is independent of the wavelength, λ. The factor μ_a'/μ_a, however, will depend upon λ unless one of the following provisions is met: (a) the absorbing element in the wedge is the same as the absorbing element in bone, whereupon $\mu_a'/\mu_a=1$; (b) the roentgen-ray spectral distribution and the absorbing element in the wedge are so chosen that the scattering absorption is negligible compared to the fluorescent absorption both in the bone and in the wedge, whereupon

$$\frac{\mu_a'}{\mu_a}=\frac{B'Z'^4\lambda^3}{BZ^4\lambda^3}=\left(\frac{B'}{B}\right)\left(\frac{Z'}{Z}\right)^4,$$

as indicated by equation (3); and (c) the spectral distribution and the absorbing element in the wedge are so chosen that the fluorescent absorption is negligible compared to the scattering absorption both in the bone and in the wedge, whereupon:

$$\frac{\mu_a'}{\mu_a}=\frac{A'Z'}{AZ}.$$

In the present technique, the first condition is satisfied essentially, since μ_a'/μ_a is made independent of wavelength for any spectral condition by using ivory for the wedge so that calcium is the principal absorbing element both in the bone and in the wedge. The second condition is satisfied also within a close approximation by the use of a continuous roentgen-ray spectrum having a short wavelength limit sufficiently great that scattering absorption is relatively small.

The second assumption, that there is only a single absorbing element in the bone and the wedge, will now be considered. Let there be m absorbing elements appearing in the bone or in the wedge, or in both. Since the roentgen-ray absorbing properties of an atom are essentially independent of its state of chemical combination equation (10) can be generalized as follows:

$$(12)\qquad \sum_{k=1}^{k=m}[\mu_k\bar{\rho}_k(x)F(x)]=\sum_{k=1}^{k=m}[\mu_k\rho_k'G(x')]$$

In this equation, subscript k denotes the k'th absorbing element. In connection with the problem of determining the density of living bones from roentgenograms, it is of interest to consider the effect on determination of the density of calcium, the principal absorbing element both in bone and ivory, of the presence of incidental absorption due to other elements. Let $k=1$ for calcium. Then, if the calcium determination is to be correct, as given in equation (11),

$$(13)\qquad \bar{\rho}_1(x)=\frac{G(x')}{F(x)}\rho_1'.$$

Subtracting equation (13) from equation (12),

$$(14)\qquad \sum_{k=2}^{k=m}\mu_k[\bar{\rho}_k(x)F(x)-\rho_k'G(x')]=0.$$

Equation (14) is satisfied by

$$(15)\qquad \bar{\rho}_k(x)=\frac{G(x')}{F(x)}\rho_k'$$

for any value of wavelength. This result indicates that, in order for equation (13) to hold for any value of λ, other absorbing

elements present must be found in the same proportion to calcium in the bone as in the wedge. Adherence to this condition cannot be established conveniently for living bones, that is bones in living human beings or animals, where it is not practicable to determine the proportion of other elements for a specific bone with great accuracy. It is of interest to return to the case where scattering is very small.

It can be shown by expansion from equations (3) and (12) that, for the case where scattering is very small,

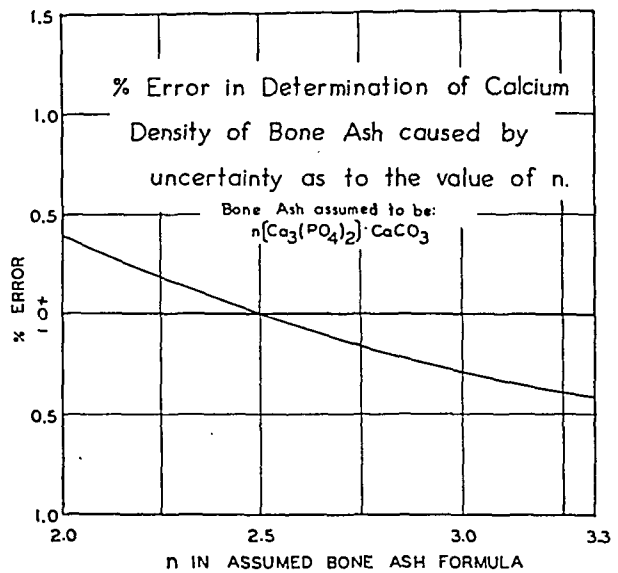


FIG. 4. Percentage error in determination of calcium density of bone ash.

$$\bar{\rho}_1(x)\left[1+\frac{\sum_{k=2}^{k=m} B_k Z_k^4 \bar{\rho}_k(x)}{B_1 Z_1 \bar{\rho}_1(x)}\right] \cong \frac{G(x')}{F(x)}\,\rho_1'\left[1+\frac{\sum_{k=2}^{k=m} B_k Z_k \rho_k'}{B_1 Z_1 \rho_1'}\right]. \tag{16}$$

This equation allows an approximate correction to be made for differences in atomic composition between the bone and the wedge. The value of ρ_1', ρ_2', ρ_3', . . . can be found from chemical analysis of the wedge material; this will fix the value of the bracketed expression on the right side of equation (16). The value of $\bar{\rho}_1(x)$, $\bar{\rho}_2(x)$, $\bar{\rho}_3(x)$, . . . cannot be determined for living bones and must be assigned median values estimated from chemical analysis of cadaver bones.

Although there is considerable controversy in the literature concerning the chemical structure of bone, there is reasonably good agreement on the atomic composition, that is, the relative quantities of each element. For purposes of determining the composition by elements, the following approximate formula is satisfactory for bone ash:

$$n[Ca_3(PO_4)_2]:CaCO_3 \qquad 2 \leqq n \leqq 3\tfrac{1}{3}.$$

For $n=2.5$, calcium is responsible for 79.60 per cent of the true absorption, phosphorus for 14.8, oxygen, 5.5, and carbon approximately 0.1 per cent. It is seen in Figure 4 that use of the median values for $\bar{\rho}_1(x)$, $\bar{\rho}_2(x)$, $\bar{\rho}_3(x)$, and $\bar{\rho}_4(x)$ corresponding to $n=2.5$ leads to less than 0.5 per cent error in the determination by true roentgen-ray absorption of the calcium density of bone ash within the expected range of variation of n.

Organic material in bone, including ossein and fat, is about 35 per cent of the total bone weight. This material is composed chiefly of carbon, oxygen, and hydrogen atoms which have smaller atomic numbers than the calcium and phosphorus in bone ash and thus have relatively small true absorption coefficients. The true absorption from this material has been estimated from equation (3) to be about 2 per cent of the true absorption occasioned by the bone ash. The classical scattering absorption, as estimated from equation (3) for the organic material, is considerably larger. Most of the scattered radiation is recovered, however, with the result that, for the roentgenographic technique under discussion, the effective absorption of the organic material is small as compared with that of the bone ash. This relationship has been verified experimentally for cadaver bones and will be the subject of further reports.

The absorption of roentgen radiation by

flesh and soft tissue is a possible source of error in the evaluation of the density of living bones by this technique. The relative absorbing power of the flesh and soft tissue is considerable under some conditions, and depends on the age of the subject, the identity of the bone cross section, and the roentgen-ray wavelength. There are some bones, such as the os calcis, where the flesh is comparatively thin and has relatively small absorptive effect. For most round bones, a simple correction can be made for flesh absorption. Specific procedures which have been developed for making flesh corrections will be described in a forthcoming report.

The various roentgen-ray absorption laws which have been cited above and which form the theoretical basis for this technique may be found in most text books on roentgen rays. The readers are referred to Clark[1], Compton,[2] Sproull,[7] and Terrill and Ulrey[9] for more rigorous statements of these laws and the limits of their applicability.

EXPERIMENTAL TECHNIQUE

Because of the difficulty of attaining high precision in locating the bone and film with respect to the roentgen tube when the roentgenogram is taken, and in locating a small spot on the film image after development, the only practical procedure is to consider not the blackness of a single spot on the bone image but instead the photographic density averaged along a linear path on the image, which represents the bone material found in a cross section of the bone along this path. This path is traced with a recording microdensitometer, and a record is secured of the photographic density as a function of the distance along the tracing path, as shown in Figure 5. Figure 6 shows the roentgenogram corresponding to Figure 5. Note that two dots are used to align the film in the microphotometer. The mineral density value obtained from analysis of a densitometer trace is the average mineral density over the cross-sectional slice of the bone defined by the tracing path, by the position of the roentgen tube at the time of exposure, and by the width of the densitometer slit opening transverse to the tracing path. This width, which is about 1 millimeter, corresponds to the thickness of the cross-sectional slice.

On the basis of experience and experimental convenience, certain selected tracing paths have been found suitable for particular purposes, and considerable care has been taken to devise standardized methods for securing uniform positioning of the bone at the time of taking the roentgenogram, and for standardizing the position of the tracing path on the film. Because the mineral density is averaged over a considerable portion of the bone volume, and because the exposure and tracing positions are carefully standardized by reference to landmarks on the bone, it is possible to reproduce mineral density values, as evaluated for the same slice of the same bone from different films, with an accuracy of a small percentage. The principal tracing paths which have been studied to date are indicated on Figures 7 and 8, although numerous others are possible.

Either a long bone, or one of the round bones serves as a subject for evaluation of mineral density indices. Certain of the long bones have been found to change during periods of certain types of undernutrition with respect to the mineral density, first at the bone metaphysis, and later in other regions. Changes are found in the width of the marrow cavity, if any, and in the density of the skeletal material itself. Such round bones as the os calcis, the ossific centers of the wrist, the patella, and others, change in mineral density with certain changes in nutritional or pathological status. The mineral density changes are believed to be essentially quantitative, without involving material alterations in the chemical composition of bone mineral.

In making roentgenograms, roentgen film of the double-coated acetate base type is used. It is necessary to employ a plumb bob or rod for locating the roentgen tube with

respect to a standard position over the part of the body being filmed, and to use a highly standardized technique of exposure and development. Tube voltages between 45 and 55 kilovolts have been found satisfactory for most work.

The following gives the essential steps involved in taking a roentgenogram and in making and evaluating a densitometer trace by the microphotometric method, using Model 4 in the series of microphotometers which have been developed since this type of measurement first was undertaken by the senior author:

Step (1). The roentgen film is made in a standard position for any part of the body which is to be used, employing an exposure energy suitable to the thickness of the object examined. A calibrated ivory step wedge is used in a standard position on each film. This is called *Film A*. A second film is taken at right angles to the first,

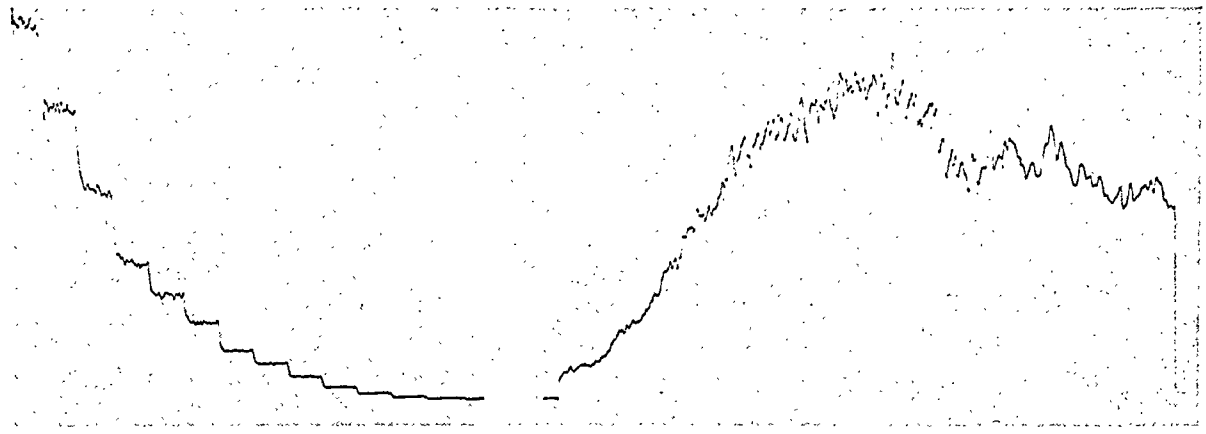


FIG. 5. Densitometer trace of os calcis.

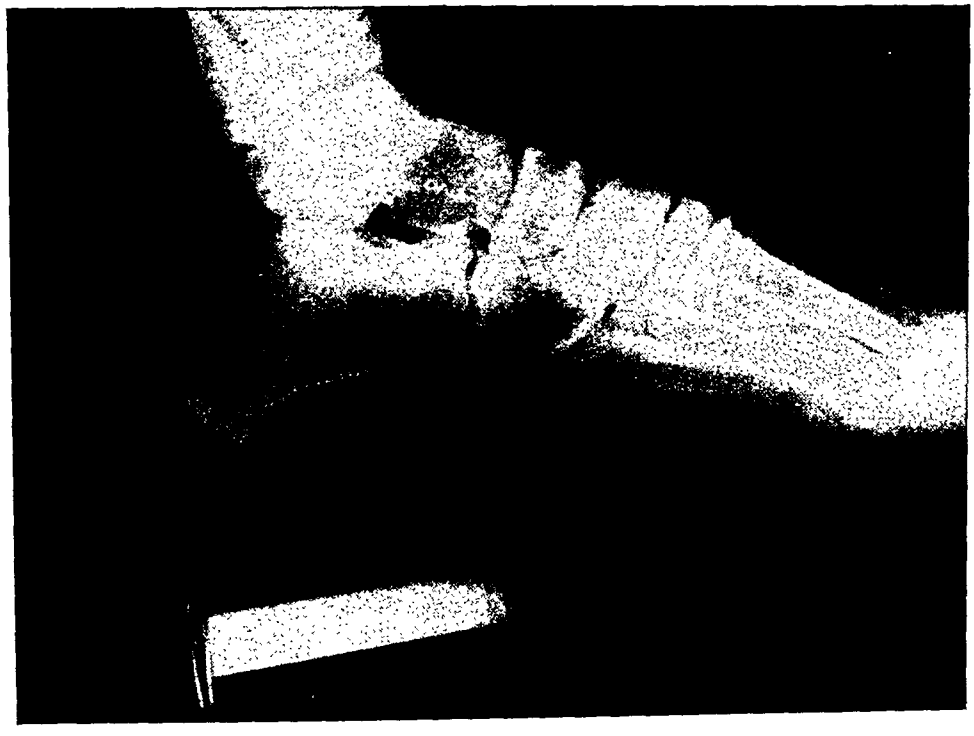


FIG. 6. Roentgenogram for densitometer trace of Figure 5.

called *Film B*. After exposure, the films are developed, fixed, and washed under as nearly uniform conditions as can be achieved.

Step (2). A contact positive is made from Film A, which is the film from which microphotometric tracings are made. In order to secure maximum reproducibility of data, systematic procedures have been evolved for establishing the exact position of the axes of the bone image along which the densitometer traces are made. The positive is used for locating tracing paths without damage to the roentgen film itself. The ends of the tracing paths then are defined on the film by means of small ink dots outside of the traced region.

Step (3). Tracings are made along the predetermined path or paths on the film, both through the bone and ivory wedge images.

Step (4). Each bone tracing is divided into a finite number of segments in accordance with a standardized procedure.

Step (5). The area under each segment of the trace is measured by means of a planimeter.

Step (6). The heights of the definable steps in the wedge tracing are measured.

Step (7). An interpolation formula is used to correct the average trace height of each segment of the bone tracing for exposure and development deviations in terms of observed height of trace and measured physical thickness of the adjacent steps on the ivory standardization wedge. The corrected segment trace heights then may be averaged to obtain a corrected average trace height value for the entire trace, expressed in units of centimeters of equivalent ivory thickness.

Step (8). Linear measurements are made both on Film A and on Film B, which enable the cross-sectional area of bone corresponding to the tracing path to be estimated. The probable cross-sectional shape of the cross sectional bone area is determined from measurements on Films A and B and from a study of cadaver bones.

Step (9). The corrected equivalent ivory

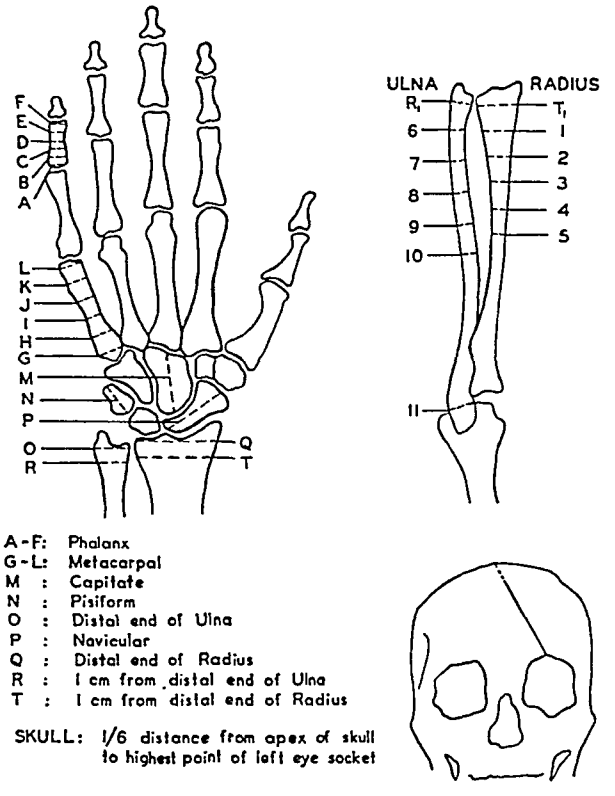


Fig. 7. Bone tracing paths.

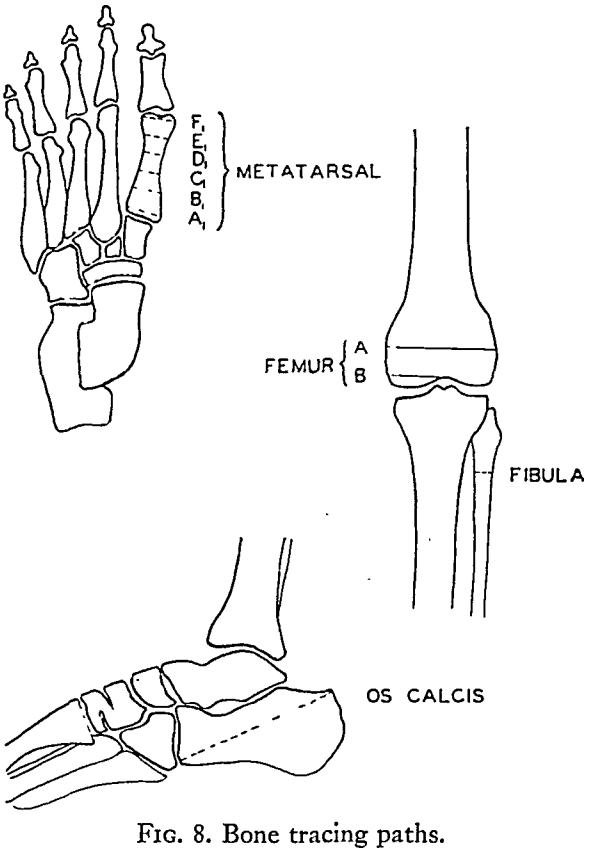


Fig. 8. Bone tracing paths.

thickness of the trace is divided by the estimated average physical thickness of bone corresponding to the microphotometer tracing path, and multiplied by the density of ivory in grams per cubic centimeter. The result is the IVORY DENSITY of the bone in grams of equivalent ivory per cubic centimeter of bone. A factor giving the ratio of bone density to density of the specific ivory wedge enables the result to be reported as bone density in grams of bone ash per unit volume.

Step (10). In certain studies Steps (8) and (9) are omitted for simplicity, and the result is expressed in terms of the average equivalent ivory thickness, in centimeters, for the bone cross section.

A precision microdensitometer, or microphotometer used in this technique, Model 4 as mentioned above, is illustrated in Figure 9; this functions essentially as follows:

A stationary beam of light passes through a lens condensing system, thence through the roentgenogram, and finally onto a photronic cell. The condensing system focuses the image of a straight filament lamp through the roentgen film and onto the photronic cell, the latter of which is in a light-tight box. The image of the brightly illuminated roentgen-ray area is focused on the plane of an adjusting slit on the near side of the photronic cell, and thence onto the cell. The latter is connected directly with a sensitive galvanometer.

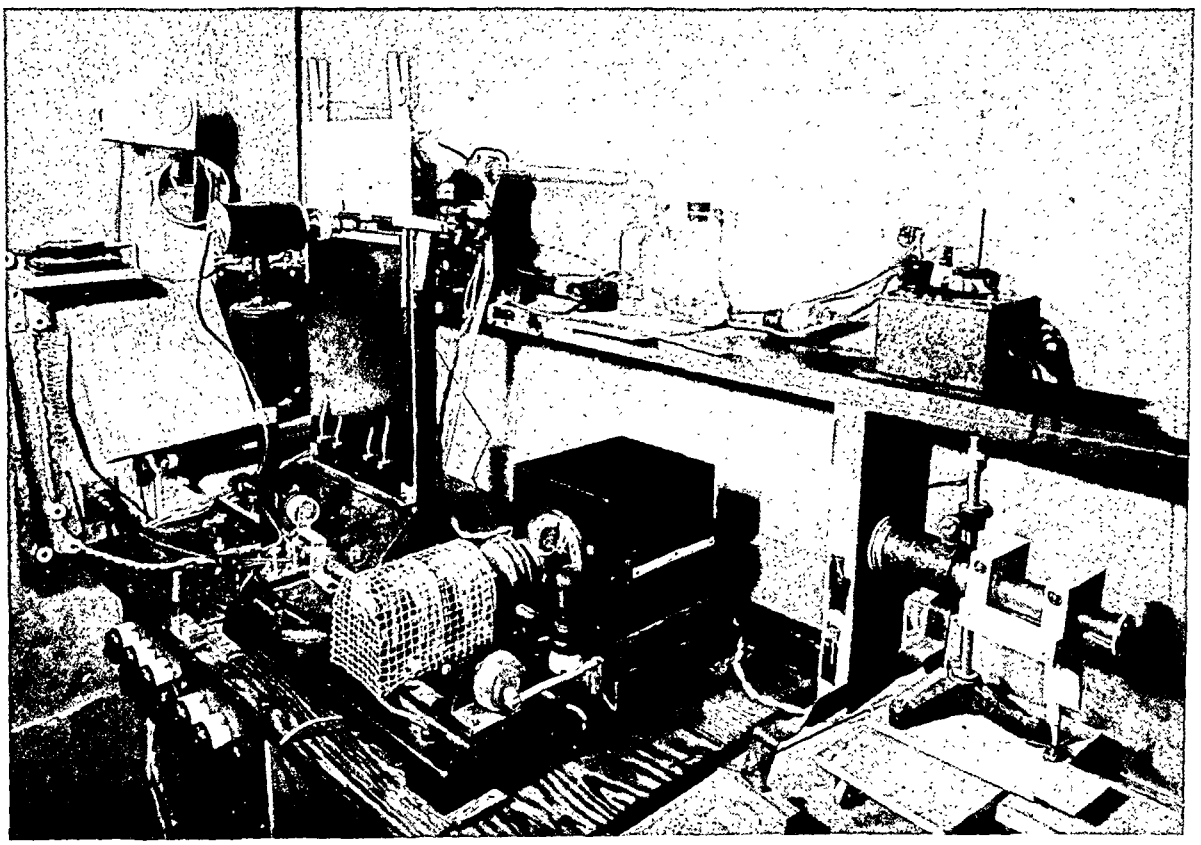


FIG. 9. Photoelectric microdensitometer (Model 4) used in making photographic tracings of mineral density in bones. (Note: Galvanometer stands at right outside of the field of the photograph.)

The film being scanned is mounted on a carriage which moves at a constant velocity of approximately 0.01 inch per second past the scanning beam. The carriage is moved by the same synchronous motor which turns the drum on which the photographic recording paper is placed. This assures a constant ratio between the linear

velocities of the carriage through the scanning beam and the surface of the recording paper. The instrument thereby is a recording densitometer.

It is essential that the intensity of the scanning lamp be controlled as closely as possible. It is operated in a direct current circuit designed to provide adequate control of the voltage across the lamp.

lens mounted so that its axis is perpendicular to the long dimension of the paper. Light is supplied to the galvanometer mirror by a suitable lamp-lens-slit system.

The height of the tracing increases with the light transmitted through the corresponding point on the roentgen film, which in turn is a determinable function of the amount of mineral matter through which

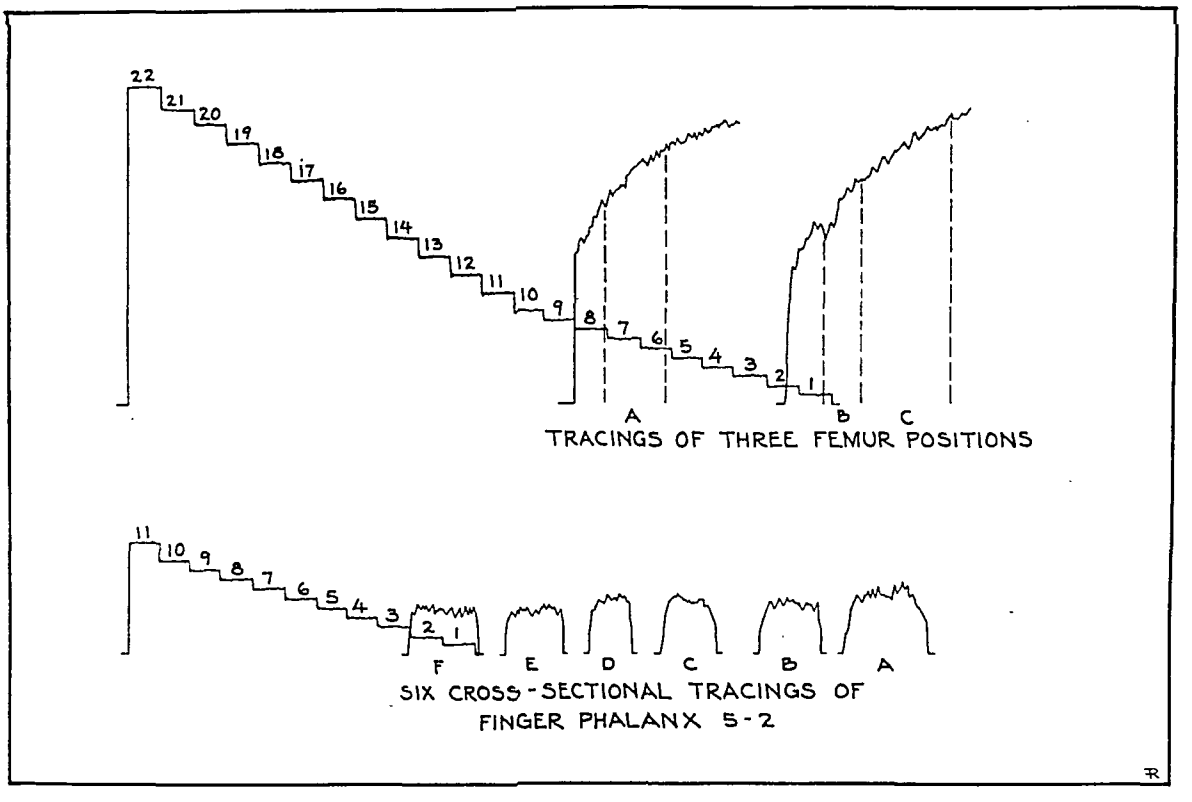


Fig. 10. Representative corrected microdensitometric bone tracings from roentgenograms (above) of three femur positions, and (below) of six cross-sectional finger phalanx 5-2.

The microphotometer must be operated in a dark room. It is convenient to use a second dark room for the processing of the photographic recording paper. The suite of laboratories used at the Ellen H. Richards Institute at present is located on a subbasement floor in a building in which freedom from external vibration is provided.

The drum accommodates recording paper up to 12 by 40 centimeters and is mounted in a housing which is light-tight. Light from the galvanometer mirror is admitted through a slot and brought to a focus on the surface of the paper by a cylindrical

the roentgen radiation has passed during exposure of the film. The area of the cross section (estimated from two exterior measurements of the bone) multiplied by the width of the path scanned on the roentgenogram image by the densitometer give a close approximation to the volume of bone for which the average mineral index is evaluated. No bone position is traced except those for which cadaver bones have been studied to assist in estimating bone shapes in directions other than the two for which roentgenograms (Film A and Film B) are taken.

Experimental checks on the reproducibility of the technique have been carried out by evaluating the Mineral Index from a number of roentgenograms prepared at the same time for the same bone under varying conditions of exposure and development. Figure 12 indicates the result of a typical series of tests in which seven identically exposed films of the ulna of a same film does not vary greatly over the wide range of development conditions considered.

It is important, however, that the exposure and development conditions be such that no part of the bone image lies either in the fog or in the black density saturation regions of the film characteristic curve, as illustrated in Figure 2, which was presented

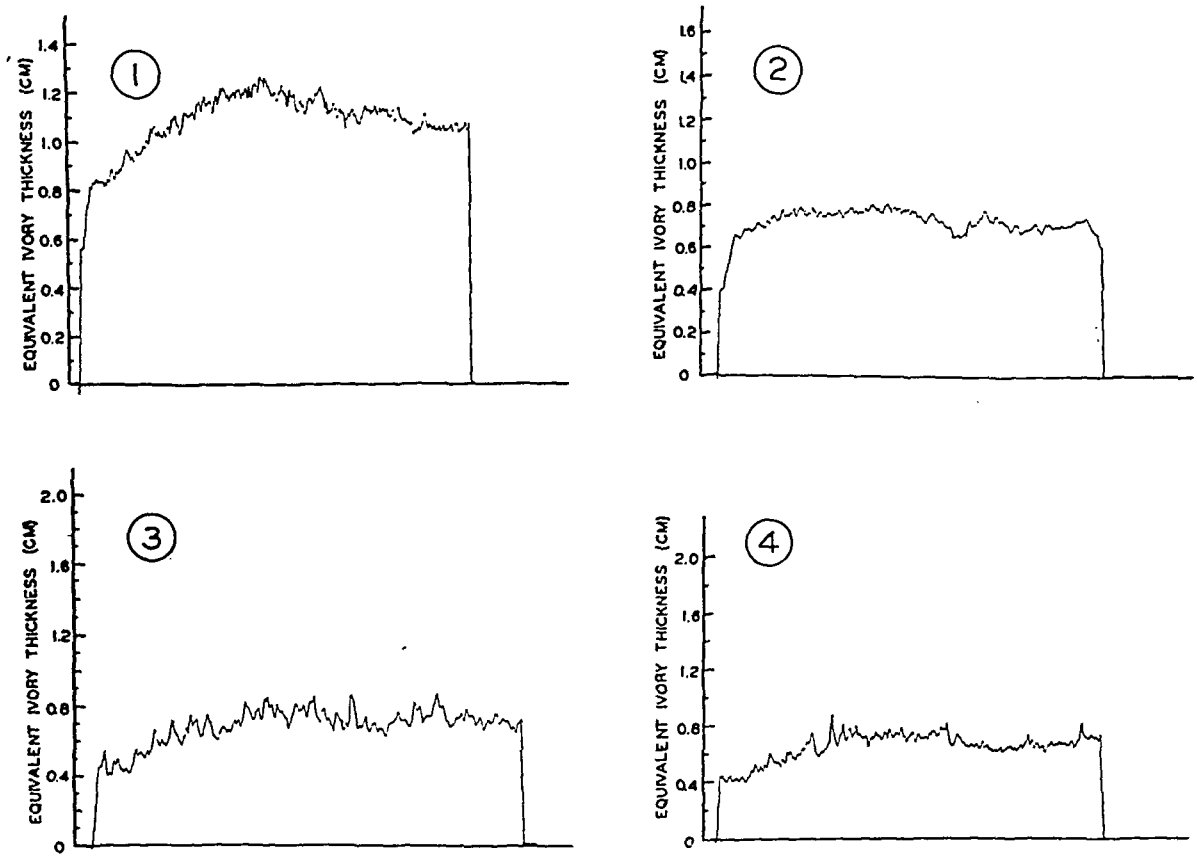


FIG. 11. Representative micro-densitometric traces of the os calcis of 4 children: (1) a well nourished male 4 years, 10 months, 8 days; (2) a slightly undernourished female 3 years, 10 months, 11 days; (3) a female transverse myelitis subject 10 years, 1 month, 12 days; and (4) a female 10 years, 10 days diagnosed as having psathyrosis (dysplasia of bone and cartilage).

child were developed for different periods ranging from two to four and a half minutes. The curve labeled A shows a wide variation with development time of the Mineral Index value which might be computed on the basis of film density alone. The curve labelled B shows that the corrected Mineral Index, obtained by correcting the density of the bone image for each film on the basis of the photographic trace of the ivory step-wedge images on the to show a typical Hurter and Driffield characteristic for photographic film.

A semi-automatic film evaluating machine of novel design (Model 5 in the Ellen H. Richards Institute series) has been constructed by the second-named author, and now is in routine use. As indicated in Figure 13, this machine comprises a densitometer, two pen and ink recorders, a function transformer, and an integrator. A trace of the ivory step-wedge image is made

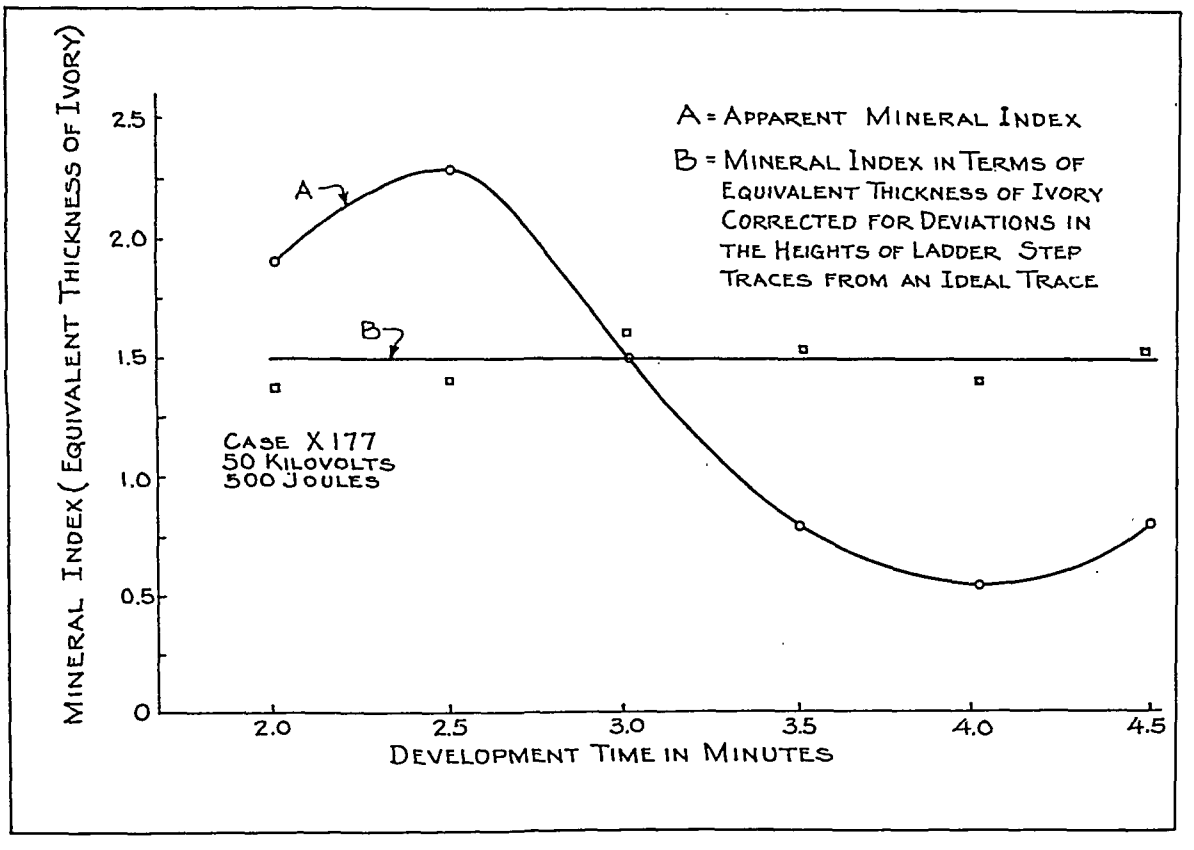


FIG. 12. Development time series on ulna.

first for each film, using the microdensitometer and first recorder, in order to determine the functional relationship between densitometer deflection and equivalent ivory thickness for that film. These data are fed manually into the function transformer. The desired bone image paths on the film then are traced. The second pen and ink recorder and the integrator are actuated continuously during the bone tracing process by the function transformer, in order to provide a corrected

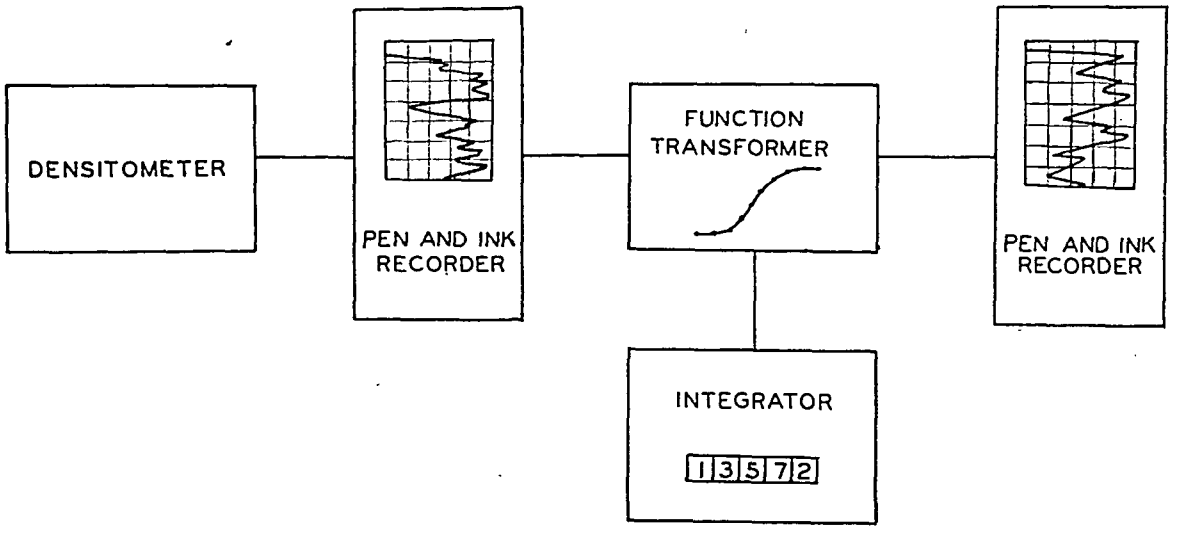


FIG. 13. Film evaluating equipment (Model 5).

equivalent ivory thickness trace and a corrected ivory cross sectional area, respectively, for the bone. The latter value, multiplied by the density of ivory and divided by the estimated bone cross sectional area gives the IVORY DENSITY of the bone, which in turn can be converted to BONE DENSITY as mentioned above.

The following gives the essential steps involved in making and evaluating roentgenograms by the semi-automatic method, using the Model 5 machine under discussion.

Steps (1) and (2). These steps are the same as those given for the Model 4 machine.

Step (3). A tracing is made along the ivory wedge image on the film.

Step (4) The heights of the definable steps in the wedge tracing are measured.

Step (5). The data obtained in (4) above are set manually into the function transformer by an operator, in order to establish the functional relationship between densitometer deflection and equivalent ivory thickness for the film being evaluated.

Step (6). The desired tracings are made along bone paths.

Step (7). During the bone tracing process, the second recorder is producing a trace, transformed automatically from the densitometer trace by the function transformer, of equivalent ivory thickness versus distance along the tracing path. Concurrently, the equivalent ivory thickness is integrated automatically along the tracing path to give a numerical value for the equivalent ivory cross sectional area of the portion of bone traced. The average equivalent ivory thickness of the cross section then is obtained by dividing the equivalent ivory cross-sectional area by the length of the tracing path.

Steps (8), (9), and (10). These steps are the same as those given above for the Model 4 machine.

APPLICATIONS

The technique described has numerous applications, many of which have not been evaluated fully as yet. In medical research studies, where measurement of the density of living bones, particularly human, is necessary, the technique should be of great utility. As a clinical tool for use in evaluating the nutritional status of an individual relative to the norm, the technique has proved in these laboratories to be of inestimable value. Comparison of successive measurements on the same individual provides a sensitive means of detecting any change in bone mineralization occasioned by changing nutritional status, by illness, or by pregnancy, and of determining the need for dietary supplements or special medical care. It is anticipated that the rate of mending of fractures or breaks can be investigated quantitatively with the help of this technique, either for medical research or for routine treatment purposes. Preliminary work indicates that quantitative study and observation of arthritic and joint calcification conditions may prove worthwhile. Soft tissue calcification following injury has been studied by this technique, as has been senile demineralization.

Aside from its applications to measurement of bone density, the technique may also be applied to quantitative measurement of the roentgen-ray absorbing power of soft tissue and flesh. Roentgen-ray absorption depends upon the chemical composition as well as upon the quantity of the material penetrated. For bone, the chemical composition is known within close limits and the density can be determined by roentgenographic means. For flesh or soft tissue the composition is not known generally, and density determination is thus not feasible. The technique as described, however, involving a recording densitometer and a standardizing step wedge, permits the average roentgen-ray absorbing power of the flesh or soft tissue associated with any selected region of a roentgenogram to be measured quantitatively in units of centimeters of equivalent ivory thickness; this gives satisfactory comparative results. Later, studies on the chemical composition of mineral deposits

in soft tissue may enable such microdensitometric measurements to be made in terms of density of actual mineral compounds.

It is well known that a modern, carefully designed densitometer is many times more accurate than the human eye for evaluating the density of photographic film. In view of this fact and of the virtual elimination of exposure and development variations effected by use of the step-wedge following the technique as described herein, it appears that the subject technique may provide a valuable tool for use by roentgenologists. A possible application of the technique to tracing injected materials in human beings and animals also exists. Where the chemical composition of the injected absorbing substance is known, it would appear feasible to determine rate of movement from a series of roentgenograms.

The authors wish to acknowledge the valuable assistance of the following staff members of The Pennsylvania State College in the development of the techniques described in this report: Ernest Axman, W. Lewis Shetler, George P. Vose, and Ruth I. Brooks.

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SUBACUTE (PSEUDOTUBERCULOUS, GIANT CELL) THYROIDITIS AND ITS TREATMENT*

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CLEVELAND, OHIO

THYROIDITIS is a relatively uncommon condition. In 1934 Cochrane and Nowak wrote, "It is no exaggeration to say that thyroiditis as an entity is unknown to the average internist and surgeon." Of the 251,072 new patients registered at the Cleveland Clinic from 1936 to 1947, a diagnosis of disease of the thyroid gland was made in 7,045. One hundred and forty-three had some type of thyroiditis and 93 had the subacute form which also sometimes is called pseudotuberculous or giant cell thyroiditis.

Apparently most reports in the literature on acute and subacute thyroiditis deal with inflammations due to bacterial infections. Table I lists several reports arranged according to the incidence of acute thyroiditis with and without suppuration.

TABLE I

Author	Year	Total Acute	Suppuration	Per Cent
Robertson	1911	96	40	42
Hagenbuch	1921	43	30	70
Burhans	1928	67	63	94
Cochrane and Nowak	1934	10	3	30
Means	1937	12	2	16
McQuillan	1938	17	6	35
Sallick	1942	12	1	8

In these reports the incidence of suppurative thyroiditis ranged from 8 to 94 per cent. In contrast to this, in our series of 143 cases of all types of thyroiditis, only 2, or less than 2 per cent, had suppuration. Bacterial thyroiditis is not the type under discussion. Suppuration does not occur in subacute thyroiditis and no organisms have been demonstrated in the tissues. The most common type of thyroiditis is a self-limiting disease, the etiology of which is unknown, though there are good reasons to suspect that viruses are responsible.

Dr. J. B. Hazard, Head of the Department of Pathology of the Cleveland Clinic, has suggested the classification for different types of thyroiditis as shown in Table II.

TABLE II

A. Specific Thyroiditis	
1. Bacterial	4
2. Parasitic	0
B. Nonspecific Thyroiditis	
1. Subacute (pseudotuberculous or giant cell)	93
2. Struma lymphomatosa (Hashimoto)	16
3. Struma fibrosa (Riedel)	11
4. Unclassified	19
Total cases	143

PATHOLOGY

The microscopic findings have been described by Hazard, as follows: The thyroid gland of subacute thyroiditis presents the following features: (1) fibrosis of variable degree, chiefly in the connective tissue partitions but also intralobular; (2) foci of small follicles with reduced or absent colloid; (3) infiltration of lymphocytes, polymorphonuclear leukocytes and plasma cells, foreign body giant cells and focal accumulations of histiocytes.

The connective tissue increase occurs as trabeculations of collagenous type of variable width and density, coinciding with anatomical partitions, and as a slight or moderate proliferation of interfollicular connective tissue separating and replacing

* From the Cleveland Clinic and the Frank E. Bunts Educational Institute. Presented at the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14–17, 1948.
† Former Fellow in Therapeutic Radiology, Cleveland Clinic.

acini. The follicles are reduced in number, small and formed by cuboidal epithelium. The lumina contain granular coagulum or a small amount of colloid frequently including collections of histiocytes. The general inflammatory infiltration is of moderate density most pronounced in the vicinity of follicles and is comprised principally of lymphocytes and polymorphonuclear neutrophils, with occasional plasma cells. Foreign body giant cells and foci of histiocytes may be frequent and usually coincide in location with follicular islands. The histiocytic foci at times contain rounded masses of colloid or may include a small collection of polymorphonuclear neutrophils. Caseous necrosis is never found. The foreign body giant cells may be large and not infrequently contain colloid masses.

CLINICAL FINDINGS

The clinical picture of subacute thyroiditis has been described by Crile and is quite typical. About one-third of our patients gave a history of recent mild upper respiratory disease. The principal complaints were pain in the neck or throat. It was quite characteristic for the pain to radiate to one or both ears. For these reasons some of our patients were examined first in the Department of Otolaryngology but no definite evidence of abnormality in the throat or ears attributable to or as a cause of thyroiditis was found. In addition to pain, patients complained of lassitude, increased fatigability, and nervousness. Weight loss, anorexia and dysphagia were common.

The onset of subacute thyroiditis in our cases was usually sudden. It nearly always developed in glands not previously noticeably enlarged but also in a few with preexisting goiters. The inflammation occasionally began in one lobe, then diffusely involved the whole gland which became swollen, firm, elastic, was movable and extremely tender, especially in early stages of disease. Regional lymph nodes were not enlarged by the inflammation. A low grade fever was usually present, seldom above 102° F. A few patients with severe reactions had chills followed temporarily by high fever. The pulse rate was often increased out of proportion to the temperature elevation. The sedimentation rate was usually elevated. In our series the basal metabolic rate ranged from minus 17 per cent to plus 30 per cent, the average being plus 10 per cent, and in only one-third was it over plus 15 per cent. White blood cell counts were normal. The whole clinical picture is one of a toxic reaction due to an inflammatory process in the thyroid gland.

All types of thyroiditis affect females predominantly. In this series only 10 per cent were males. The age incidence varied from twenty to sixty-three years, but most patients were between twenty-five and fifty-two years of age.

The natural course of the disease inclines toward spontaneous recovery without permanent damage to the gland. Some authors have stated that the condition usually subsides in a week or two. This, however, has not been our experience. Our patients presented themselves both early and late in the course of disease, many relating a history of the condition existing for two or more months. The extremes of duration were from two days to a year. Most patients remained well enough to carry on their ordinary activities although some were incapacitated by the systemic reactions and a few were so ill from extreme exhaustion, weakness, and toxicity that they were hospitalized and sent for roentgen therapy on litters.

TREATMENT

Some authors have advocated conservative treatment for subacute thyroiditis, and recommend rest, local applications of heat or cold, and administration of salicylates or thyroid extracts. We have observed no benefit from the use of sulfonamides or antibiotics. In 1945 King and Rosellini summarized a series of cases treated with thiouracil with benefit. Surgical operations are unnecessary for subacute thyroiditis. Biopsies may be made with the Silverman needle.

We began administering roentgen therapy for subacute thyroiditis in 1933. The technique has varied and is similar to that employed for other inflammatory processes. During the last few years the technique has been 200 kv., filter equivalent to 1.0 mm. half-value layer copper, 50 cm. distance and 100 or 150 roentgens skin dose every other day for four to six treatments. The size of portal may be 10 by 10 cm. or large enough to irradiate the entire gland.

Our colleagues in the Divisions of Medicine and Surgery agree that roentgen therapy is the best form of treatment. Crile wrote, "Subacute thyroiditis responds promptly and completely to roentgen ray therapy." Most patients were relieved of pain and tenderness after two or three treatments, the severity of other symptoms was reduced and the course of the disease shortened. Recurrence of symptoms in mild form developed in a few patients and were relieved by a second course of roentgen therapy. We have observed no deleterious effects from treatment; myxedema has not resulted, and the dosage is too small to cause skin reactions.

TABLE III

Cured with one course of roentgen therapy	40
Improved and second course followed by cure	6
Recurrences, no second course given	1
Untraced after treatment	8
Total cases	55

A possible explanation of the beneficial effects of roentgen therapy for subacute thyroiditis is supported by Lea's experiments proving that viruses are inactivated by radiation. We have shown similar beneficial effects with roentgen therapy for encephalitis attributed to virus disease.[17]

Of 93 of our cases having a diagnosis of subacute thyroiditis, 55 had roentgen therapy. The treatment was advised for 7 but we have no record of their having received it. They may have been treated elsewhere. Operation was performed on 14 and the diagnosis established by microscopic examination of tissues removed. Other methods of treatment were used for 17 cases. No information was obtainable about results in 8 cases. The results in cases given roentgen therapy are shown in Table III.

SUMMARY AND CONCLUSIONS

1. A series of 143 cases of thyroiditis seen at the Cleveland Clinic from 1936 through 1947 has been reviewed from the standpoints of incidence and classification.

2. The pathologic and clinical manifestations and diagnosis of subacute thyroiditis have been discussed.

3. The results of roentgen therapy for 55 cases of subacute thyroiditis have been presented.

4. Roentgen therapy is indicated and has been proved beneficial for subacute thyroiditis.

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DISCUSSION

Dr. Hugh F. Hare, Boston, Mass. I am pleased to hear this paper and to congratulate the authors on presenting us with the first group of patients with thyroiditis treated by irradiation. There have been a few sporadic reports but none revealing such large groups of cases. The course of the disease is limited and the patients tend to recover whether treatment is given or not. Certainly the relief of symptoms that they have obtained makes treatment more worthwhile and, too, they show that the course of the disease is shortened. Surgical intervention has been used, but not as satisfactorily, as reports show that myxedema occurs in 50 per cent of cases thus treated. Drs. Osmond and Portmann have really shown improved methods of handling these cases. I hope that they will go further than they have and try to differentiate the different types of thyroiditis.

SARCOMA OF THE UTERUS

A REPORT OF NINE CASES*

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SARCOMA of the uterus was first described clinically by Mayer in 1860 and one of his cases was confirmed pathologically by Virchow two years later.[9] Since that time there has been a voluminous literature which included several reports discussing the place of radiation therapy in the treatment of this condition. These reports are remarkable for the great differences in their evaluation of radiation therapy. The obvious reason for this difference of opinion is that it is extremely difficult to get a large enough series of patients so that a definite report can be written. There are also great variations in the methods of radiation therapy and of reporting results. As a consequence, it was decided to review the experience in the Radiation Therapy Department of Bellevue Hospital in an attempt to evaluate the effectiveness of radiation in the treatment of uterine sarcoma.

INCIDENCE

The incidence of sarcoma of the uterus is reported as varying from 0.5 per cent to 5.0 per cent of all malignant growths of the uterus.[7,10,14] Our series consists of 9 proved cases out of a total of 1,627 cases of malignancy of the cervix and corpus, an incidence of 0.56 per cent.

The range of ages as reported in the literature is extremely wide. The average seems to fall between the fifth and sixth decades. In our series the ages range from seventeen to sixty-eight years, with an average of 49.3 years. The average age of cases of carcinoma of the corpus in our series was 58.9 years.

In the series of cases reported in Veit's Handbuch[14] one-quarter of the patients were nulliparous and three-quarters parous. In our series 8 of the 9 cases were parous.

One of the most important problems discussed in the literature is the incidence of sarcomatous degeneration of fibroids. Many fibroids show marked cellularity and it is difficult to tell histopathologically when they are truly sarcomatous. The reported incidence varies from 0.4 per cent to 10.0 per cent. The figure most generally accepted is that 1 per cent of all myomas show sarcomatous degeneration.[5] Obviously this difference in diagnostic criteria causes a great variation in the reported results.

Corscaden and Stout[4] found that, despite the many thousands of cases of fibroids of the uterus treated with irradiation, only 4 cases of sarcoma were reported as occurring in this group. They concluded that the only safe criteria for the diagnosis of sarcoma arising in a fibroid is infiltrative and destructive growth, rather than microscopic criteria. We believe that this is a good approach to a difficult problem.

DIAGNOSIS

The symptoms do not differentiate this condition from fibroid tumors or carcinomas. The cardinal symptoms in all are hemorrhage, discharge, and pain. Pain and debility may occur relatively earlier in sarcoma than in carcinoma because of the more rapid rate of growth and concurrent necrosis. However, Smith[13] found pain to be a symptom in only two-fifths of his patients.

The physical findings are also not characteristic.

As a result, the diagnosis will rest on pathological examination. The specimens

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may be obtained by dilatation and curettage, or after hysterectomy. Most authors state that the diagnosis is usually not made until after hysterectomy. Therefore their reports do not consider preoperative irradiation as a method of treatment applicable to the problem. However, a certain percentage of sarcomas are present in the uterine cavity and are diagnosed by curettage. Wolfe[16] states that this occurred in 50 per cent of his cases. In our series the pathological diagnosis was made before hysterectomy in 4 of the 9 cases.

PATHOLOGY

Ewing[6] has divided this group of tumors into mural and mucosal sarcoma. However, in advanced cases it may be almost impossible to tell where the sarcoma arose.

In any case the cell type may have a prognostic significance. Ewing's classification included: (a) recurrent myoma; (b) spindle cell; (c) round cell.

The most benign is the relatively rare recurrent myoma which has an orderly arrangement of cells with well formed vessels.

The next most malignant group are those with spindle cells. They have granular cytoplasm, vesicular nuclei, and occasional giant cells. They invade the parametrium, broad ligaments and mucosa with ulceration, necrosis, and cachexia.

Those sarcomas which are composed primarily of round cells are even more malignant. They grow rapidly, and quickly produce local destruction, cachexia and metastases.

Novak and Anderson[10] added a mixed cell group which is more malignant than those previously mentioned.

Ewing believed the entire group to be of myogenic origin. However, he stated that there is evidence that endometrial sarcomas may arise from stroma cells.

Carcinosarcoma is another type that has been discussed in many reports. It is still an ill-defined entity. Ewing believed that many of the cases reported were due to atypical growth of the epithelial cells or atypical reactions of the stroma, since the metastases were usually shown to be carcinomatous. Case IX in our series illustrates the difficulty of making this diagnosis.

Gessner[14] found distant metastases in 24 of 33 autopsied cases. These included metastases to the lungs in 15 cases, to the liver in 10 cases, to the intestine in 8, to the omentum in 5, to the kidney in 5, to the pleura in 5, and a smaller number in other organs.

Brooke and Thomason[3] found only four reports in the literature of bone metastases which were demonstrated on roentgenograms. Case VIII in this series had a metastasis to the skull (Fig. 1).



FIG. 1. Case VIII. Roentgenogram of skull showing area of metastasis. This region has been overexposed to show the bony spicules and soft tissue detail.

REVIEW OF METHODS OF TREATMENT AND PROGNOSIS

The reports in the literature are not strictly comparable because of the varied criteria for malignancy in fibroids. As a consequence, no attempt has been made to present an exhaustive review of the literature. Some of the outstanding articles have been abstracted to illustrate the confusion that exists about the value of radiation therapy in the treatment of sarcoma of the uterus.

Every article is in complete agreement that the primary means of treating this condition is early, complete surgery. Never-

theless there are several reports of cases treated by irradiation alone.

Seitz and Wintz[12] in their report found that 4 of 8 inoperable cases treated with roentgen therapy were well for three years without evidence of recurrence. Béclère[1] culled 9 cases from the literature which were treated by irradiation and were without recurrence from two to seven years after treatment. Both of these reports were quite enthusiastic as to the effectiveness of irradiation.

On the other hand, Regaud and Lacassagne[11] treated 6 inoperable cases by irradiation. They found that 5 of these died within six months and only one was well for three and a half years. As a result, they felt that irradiation alone was of little value in the treatment of uterine sarcoma.

Masson[8] reported that 72 per cent of cases with sarcoma in a fibroid survived three years after operation.

Bosse and Stanton[2] found that none of their 13 cases with evidence of invasion survived five years despite radiation therapy, while 12 of their 14 cases without evidence of invasion were well for five years.

Smith[13] found that none of his 24 patients survived more than four years. He felt that irradiation had no effect whatever on the course of the disease.

Kimbrough,[7] in his excellent statistical study of 43 cases, reported a total five year survival rate of 34.3 per cent for 35 of his cases. The operative mortality in his series was 4 out of 36 patients. Only a few of his cases received radiation therapy. However, he reported one case that was treated for recurrence and was well for six years after radiation therapy.

Novak and Anderson[10] prefer a panhysterectomy followed by irradiation. They reported 15 of their 50 cases well after five years, with 3 additional deaths before ten years. The operative mortality in their series was 7 out of 50 cases.

Von Kovesligethy[15] reported 32 cases in which panhysterectomy was done in 20 followed by radiation therapy. Five of these survived five years. Two of the 12 patients treated with irradiation alone survived five years. He felt that those cases which did not survive five years showed good palliative results.

We feel that preoperative radiation therapy should be used in all cases diagnosed by curettage. This should preferably be in the form of intrauterine radium, and should be followed by panhysterectomy in six to eight weeks. All cases, whether treated preoperatively or not, should have intensive postoperative deep roentgen therapy. In advanced cases, palliative radiation therapy should be administered.

REPORT OF CASES

Group A. Cases in which combined surgery and irradiation were used.

CASE I. C. M., a colored housewife, aged fifty-eight, was admitted in July, 1931, with a chief complaint of vaginal bleeding and intermittent lower abdominal pain for four months. Menstruation started at fourteen years and occurred every thirty days for four days' duration. Menopause occurred at the age of forty-five. She was gravida IV, para III, with one uncomplicated instrumental abortion at two and one-half months.

The diagnosis on admission was fibromyoma of the uterus, and a supracervical hysterectomy was performed.

Pathological study of the removed organs showed the wall of the uterus to be 2 cm. thick, smooth and streaked yellowish red. A large, yellowish red, irregular mass of tissue projected into the lumen from the posterior wall of the endometrial cavity. This completely filled the cavity. This tissue was very friable and revealed soft, yellowish white, and in spots hemorrhagic core on section. Microscopic diagnosis was mixed spindle and round cell sarcoma.

Treatment and Course. Postoperative roentgen therapy of 100 per cent skin erythema dose was given to four 10 by 15 cm. pelvic fields. (This was the unit of dosage in use at that time.) The factors were: 200 kv., 5 ma., with 0.5 mm. Cu plus 0.9 mm. Al filter, at 80 cm. distance. Half-value layer 0.9 mm. Cu.

The results in this patient were not ascertained because she did not return for further treatment or follow-up.

CASE II. L. M., a white female, unmarried, aged seventeen, was admitted to our service in

November, 1935, with a chief complaint of pain in the left lower quadrant for one month. Menstruation started at fourteen years and occurred every twenty-eight days for four days' duration. She had never been pregnant.

Physical examination on admission revealed the cervix to be posterior and the uterus forward, firm, and enlarged to 2 cm. above the symphysis. It was quite movable and no adnexal thickening was palpable.

Dilatation and curettage showed an irregular cavity with bits of necrotic tissue, but a pathological diagnosis was not made. Following this a supracervical hysterectomy was done.

Pathological examination showed the uterus to be 6 by 10 by 10 cm. in size. The surface was covered by smooth pink serosa except for an area on the right superior anterior aspect at which place there was a soft, shaggy, friable mass projecting through the serosa through an opening 6 cm. in diameter. On each lateral aspect of this there was a subserous swelling measuring 3 by 4 cm. Filling the uterine cavity was a ragged necrotic mass which measured 3 by 6 cm., the tissue of which resembled that projecting through the anterior wall.

Microscopically the greater part of the tissue was pale blue cells which infiltrated the stroma in all directions. The cells had fairly large pale blue vesicular nuclei with a relatively small amount of cytoplasm with indistinct cell outlines. Many mitotic figures were seen. The diagnosis was sarcoma of the uterus.

Treatment and Course. The patient was given 750 r (measured in air) over two 10 by 15 cm. anterior pelvic fields and 600 r (air) over two 10 by 15 cm. posterior pelvic fields. The small amount of therapy was due to the patient's refusal to continue treatment. After six months, however, she returned to the clinic at which time she was given an additional 450 r (air) over each of the four areas. The factors were: 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at a distance of 40 cm. Half-value layer 0.9 mm. Cu.

This patient has been followed up to the present time (1948) and is without complaint or evidence of recurrence. The total survival time is thirteen years.

Case III. M. S., a white female, married, aged forty-six, was admitted to our service in July, 1937, with a chief complaint of vaginal bleeding for three years. This took the form of gradually increasing menstrual periods. She had been operated upon one year before at another hospital and was told that she had tumors of the uterus but not all of them were removed. She continued to have menstrual as well as intermenstrual bleeding after that operation. Menstruation started at seventeen years and occurred every twenty-eight days for seven days' duration. She was gravida VII, para VI with one spontaneous abortion at four months.

Physical examination showed the fundus to be irregular and enlarged half way to the umbilicus. The cervix, parametria and adnexa were apparently normal. Her hemoglobin was 3.5 gm. and red blood cell count 1,500,000.

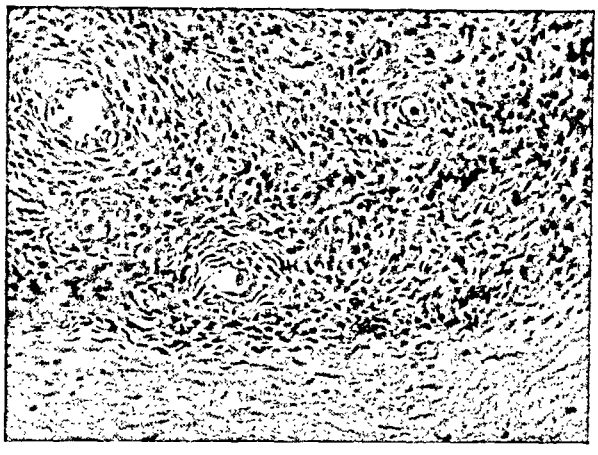


Fig. 2. Case III. Well differentiated sarcoma of uterus.

After several transfusions a supracervical hysterectomy, bilateral salpingo-oophorectomy, and excision of the right infundibulopelvic ligament was performed. This ligament was excised because there was gross evidence of tumor invasion.

Pathological examination showed the uterus to be enlarged to three times normal size and to be nodular. Some of these nodules were due to intramural fibroids. Extending through the right side of the uterus was a soft neoplastic growth which appeared to be malignant tissue and which extended into the blood vessels of the broad ligament and right infundibulopelvic ligament. The tumor was cut across at the right broad ligament. Histopathologically the cells were not very malignant but extension into the extrauterine tissue was unquestionable (Fig. 2).

The diagnosis was sarcoma of the uterus, arising from endometrial stroma, cut across at the broad ligament.

Treatment and Course. Postoperatively the patient was given 1,500 r (air) to each of two 20 by 20 cm. anterior pelvic fields; 1,800 r (air) to

each of two 20 by 20 cm. posterior pelvic fields; and 1,350 r (air) to each of two 20 by 20 cm. lateral pelvic fields. The factors used were: 200 kv., 20 ma., with 0.5 mm. Cu. plus 1.0 mm. Al filter, at 50 cm. distance. Half-value layer 0.9 mm. Cu. The estimated tumor dose was 2,250 r in a period of forty-five elapsed days.

She was followed without evidence of recurrence until September, 1941, when she moved to another city and was lost to follow-up. This patient was well for the four years and two months she was followed in the radiation therapy clinic.

This case illustrates the importance of postoperative irradiation. There was a long survival despite the fact that not all the tumor tissue was removed by surgery.

CASE IV. C. G., a white widow, aged forty-nine, was admitted to the gynecological service in April, 1945, with a chief complaint of intermenstrual bleeding for two weeks before admission associated with a steady severe pain in the left lower quadrant. Menstruation started at thirteen years and occurred every twenty-eight days for five days' duration. She was gravida IV, para IV.

On admission, physical examination revealed a parous introitus. The cervix was dilated two fingers. The fundus as such was not outlined but was incorporated in a firm irregular mass the size of a four to five month gestation. The mobility of this mass was limited. The adnexa and parametria were free. Speculum examination showed the cervix to be patent and a foul necrotic mass was seen protruding from the external os.

The patient had a supracervical hysterectomy and bilateral salpingo-oophorectomy for supposed fibromyomas of the uterus.

Pathological examination showed that the uterus measured 12.5 by 10 by 7 cm. The surface was smooth but the contour was irregular due to the presence of a large intramural fibroid, measuring 7 cm. in diameter. On section it had a yellowish appearance and the consistency was rubbery. Several other intramural fibroids were present varying in size. The endometrial cavity was greatly distorted by a large pedunculated submucous fibroid 8 cm. long and 5 cm. in diameter.

Microscopically sections through the submucous fibroid showed hyalinization, necrosis, liquefaction, and calcification. Sections through the waxy intramural fibroid showed great variability of cells with anaplasia, mitosis, and invasion into blood sinuses.

The pathological diagnosis was sarcoma of the uterus.

Treatment and Course. Roentgen therapy consisting of 2,000 r (air) to four 20 by 20 cm. pelvic fields was administered in thirty-five elapsed days. The factors were: 200 kv., 20 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 50 cm. distance. Half-value layer 0.9 mm. Cu. The estimated tumor dose was 2,500 r to each parametrium.

The patient has been followed without complaint or evidence of recurrence until the present time (1949). The time followed to date is three and one-half years.

CASE V. A. W., a widowed colored woman, aged thirty-four, was admitted to the gynecological service in October, 1947, with a chief complaint of low back pain for seven months and swelling of the abdomen for three months. She had a 35 pound weight loss over this period. Menstruation started at fourteen years and occurred every thirty days for three days' duration. She was gravida III, para II, with one spontaneous abortion at five months.

Physical examination on admission revealed a symmetrical firm abdominal mass arising from the pelvis which was palpable to a point 1 cm. above the umbilicus. The cervix was firm, posterior and closed. There was no bleeding from the cervix although it was apparently attached to the mass above. No separate masses were palpable.

Roentgenography revealed small and large nodular infiltrations of both lungs. The findings were those of metastasis (Fig. 3).

Exploratory laparotomy was done with a diagnosis of ovarian carcinoma. A large tumor mass was found attached to the uterus, left ovary and omentum. Complete removal was impossible, but the greater part of the lesion was removed.

Pathological examination showed that the specimen was a supravaginal portion of the uterus incorporated in an irregular lobulated 25 by 23 by 22 cm. mass. The endometrial cavity was filled with necrotic brown material apparently arising from the endometrium. The wall of the uterus was broken through in several places and in direct communication with large irregular tumor lobules which arose from all sides of the corpus. The surface of the tumor showed no definite capsule.

Microscopically the endometrium and portion of the myometrium were completely replaced by highly undifferentiated anaplastic

cells. These were in general of the spindle cell type. However, there were round cells in all areas. The nuclei showed marked hyperchromatism and variation in size and shape. Mitoses were numerous.

The pathological diagnosis was sarcoma of undetermined type, probably leiomyosarcoma of the uterus.

The patient had a very stormy postoperative course. When she recovered her only complaints were severe pain in her chest and moderate cough.

Roentgen examination again revealed the nodular infiltration of both lungs.

At this time she was given a course of 5 mg. of nitrogen mustard intravenously over a four day period. This had no effect on the size of the metastases or the severity of her symptoms.

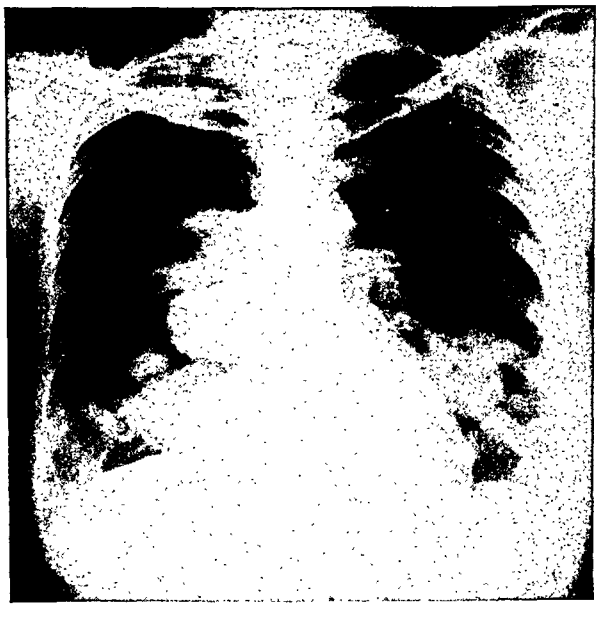


FIG. 3. Case V. Roentgenogram of chest showing nodular densities in both lung fields.

Following this the patient was treated with roentgen therapy and was given 1,800 r (air) to an anterior and a posterior 10 by 15 cm. right mediastinal field. The factors were: 200 kv., 20 ma., with a Thoraeus filter, at 50 cm. distance. Half-value layer 2.0 mm. Cu. The estimated tumor dose was 1,430 r to the mediastinum in sixteen days. After this course the patient's pain completely disappeared, although her cough was only slightly improved. Roentgenograms showed no change in the size of the lesions in the chest. This represents an excellent palliative response to roentgen therapy after nitrogen mustard therapy had proved ineffective.

Group B. Inoperable cases which were treated by irradiation alone.

CASE VI. F. M., a housewife, married, aged sixty-five, was admitted to our service in September, 1925, with a chief complaint of severe pain in the lower abdomen and vaginal bleeding for three days before admission. Menopause occurred at the age of forty-eight. She was gravida 1, para 1. No further menstrual history is available.

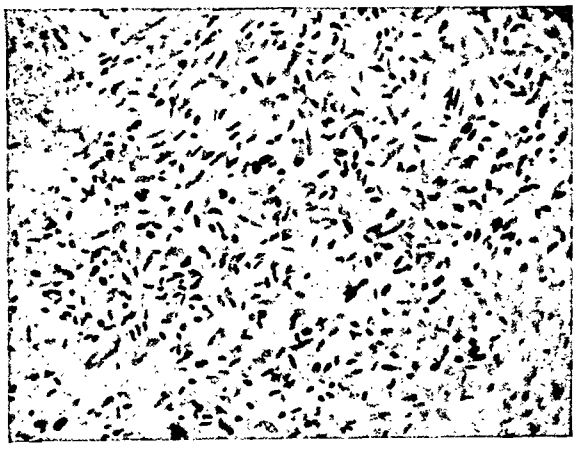


FIG. 4. Case VI. Spindle cell sarcoma.

On admission the cervix was soft, irregular, and patulous. Uterus and adnexa were not palpable. Speculum examination revealed a bloody discharge coming from the cervix.

Dilatation and curettage was done and the pathological report was spindle cell sarcoma with an occasional giant cell (Fig. 4).

Treatment and Course. Operation was contraindicated by the age and general condition of the patient. She was treated only with radiation therapy.

In August, 1925, a tandem of four tubes of radon filtered with 1 mm. platinum was inserted into the uterus for a total of 3,724 millicurie-hours. This was followed by roentgen therapy of 50 per cent skin erythema dose to anterior right and left 10 by 15 cm. pelvic fields, and 75 per cent skin erythema dose to posterior right and left 10 by 15 cm. fields. (The skin erythema dose was the unit in use at that time.) The factors used were: 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 40 cm. distance. Half-value layer 0.9 mm. Cu.

She was well until June, 1927, when she had a recurrence of bleeding for two days. She was treated with a radium tandem as before for an additional dosage of 3,132 mc-hr.

The patient was well until January, 1928,

when she began to bleed from the cervix again. Curettage at this time revealed sarcoma. Another radium tandem was inserted for a dosage of 2,879 mc-hr.

The patient was followed without complaint until March, 1928. At that time she did not return to the clinic. The time followed was two and a half years. This illustrates a good palliative result from radiation therapy alone.

CASE VII. S. B., a housewife, aged sixty, admitted in June, 1933, with a chief complaint of vaginal bleeding for five months. She was bedridden from the anemia as well as her rheumatoid arthritis. Menstruation started at fourteen years and occurred every twenty-eight days for four days' duration. Menopause occurred at age of fifty. She was gravida V, para III, with two spontaneous abortions at five and five and one-half months.

Physical examination showed that the patient had severe generalized rheumatoid arthritis and severe anemia.

Gynecological examination revealed a two finger introitus with a relaxed pelvic floor. There was a moderate cystocele and rectocele. The cervix was shortened and patulous. It admitted the tips of two fingers. The fundus was not palpable because of a tense abdomen but the adnexa appeared to be free. On speculum examination the rim of the cervix was easily pushed apart and large meaty clots of blood and tissue were easily removed from the cervical canal.

The pathological report of these clots was spindle cell sarcoma.

Treatment and Course. Because of her poor general condition this patient was treated by irradiation alone. She was given 800 r (air) to each of two 10 by 15 cm. anterior pelvic fields and 1,000 r (air) to each of two 10 by 15 cm. posterior pelvic fields. The factors were: 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 40 cm. distance. Half-value layer 0.9 mm. Cu.

Following this a sound containing three tubes of 15 mg. radium each filtered with 1.5 mm. platinum and a colpostat and cork with a 10 mg radium tube filtered with 2.5 mm. platinum in each cork were inserted into the uterus and vagina. The total dosage was 4,320 milligram-hours in the uterus and 1,920 mg-hr. in the vagina.

One month later she was given another course of roentgen therapy of 1,200 r (air) to four 10 by 15 cm. pelvic fields. She was also given 2,000 r (air) to both suprapubic and sacral areas, of 10 by 15 cm. each. Factors used were 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, 40 cm. distance. Half-value layer 0.9 mm. Cu.

The patient improved markedly and was up and about. Her fundus remained two fingers above the symphysis and a slight serosanguineous discharge persisted. In April, 1934, she moved to another city and was lost to follow-up. Time followed was ten months. This patient had a good palliative effect despite her poor initial condition.

CASE VIII. B. M., a housewife, aged fifty-eight, was admitted in October, 1933, with a chief complaint of vaginal bleeding for ten months. Nine months before a diagnosis of sarcoma had been made and she was treated with intrauterine radium at another hospital (amount unknown). Bleeding continued and the patient developed lower abdominal pain. At this time she was admitted to our service. Menopause occurred at forty-six. She was gravida XVIII, para XIII. Further gynecological history was not obtained.

Physical examination showed a chronically ill patient. The cervix was clean and the uterus retroflexed. There was tenderness and fullness in both fornices. The rectum was so narrowed and tender that rectal examination was impossible.

Treatment and Course. A dilatation and curettage was done. Following this a sound containing three tubes of 15 mg. each of radium filtered with 1.5 mm. platinum was inserted into the uterus for a dosage of 6,345 mg-hr.

Pathological diagnosis of the curettings was mixed spindle and round cell sarcoma.

She improved only slightly and two months later developed severe headaches. Examination revealed a mass attached to the skull. Roentgenogram showed an osteoblastic osseous change about 2 cm. across, situated 5 cm. posterior to the bregma. The bony deposit was perpendicular to the external table (Fig. 1).

This area in the skull was treated with 25,000 mg-hr. with the 5 gram radium pack at a distance of 6 cm., with a filtration of 5.0 mm. lead and 0.5 mm. platinum. This was followed by 1,200 r (air) to each of four 10 by 15 cm. pelvic fields and 2,000 r (air) over the skull lesion. The factors were 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 40 cm. distance. Half-value layer 0.9 mm. Cu.

There was no improvement. The patient's course was retrogressive following therapy and she died in September, 1934.

Autopsy revealed a sarcoma arising in a

uterine fibroid with pulmonary and pleural metastases. There were also metastases to the liver, mesentery, ovaries and ribs.

Total time followed with disease was one year and five months.

This patient had little relief from radium or roentgen therapy.

This is the fifth case reported in the literature with bone metastases from a uterine sarcoma demonstrated on roentgenograms.*

Case ix. M. T., a housewife, aged sixty-one, was admitted to our service in October, 1937, with a chief complaint of spotting of bright red blood for fifteen months. For four months this had been accompanied by a sharp pain in the right lower quadrant. Menstruation began at thirteen years and occurred every thirty days for seven days' duration. Menopause occurred at the age of forty-five. She was gravida vii, para vii.

Physical examination revealed an acutely and chronically ill patient. The abdomen was tense and a fluid wave was present. The cervix was atrophic and the parametria soft. The uterus was not palpable. Rectal examination revealed a large, firm, cystic mass in the cul-de-sac. This was about 10 to 15 cm. in diameter and seemed to originate in the left adnexa.

A curettage was performed and pathological examination of the curettings revealed a compact arrangement of strands, cords, and nests of an epithelial type of cell growing in a totally irregular fashion in a fibrous tissue stroma. Cells were large with poorly defined outlines, but with an abundant cystoplasm. Nuclei were large, varied in size and shape, and were pale staining. Distinct mitoses were seen in the majority of nuclei. In other areas the cells were of a spindle cell type, with smaller deeply staining nuclei, and retaining their compact cellular arrangement (Fig. 5 and 6).

The pathological diagnosis was transitional cell epithelioma showing in several places highly suspicious signs of a genuine spindle cell sarcoma.

Treatment and Course. The patient was very weak and received only 750 r (air) to each single 20 by 20 cm. anterior and posterior pelvic field. The factors were 200 kv., 5 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 80 cm. distance. Half-value layer 0.9 mm. Cu.

On completion of therapy the patient signed out of the hospital and did not return.

* Since this report we have had another case with a mixed osteoplastic and osteolytic metastasis to a lumbar vertebra.

This is presented as a possible case of carcinosarcoma.

COMMENT

These 9 cases include 2 in which apparently complete removal of the tumor was

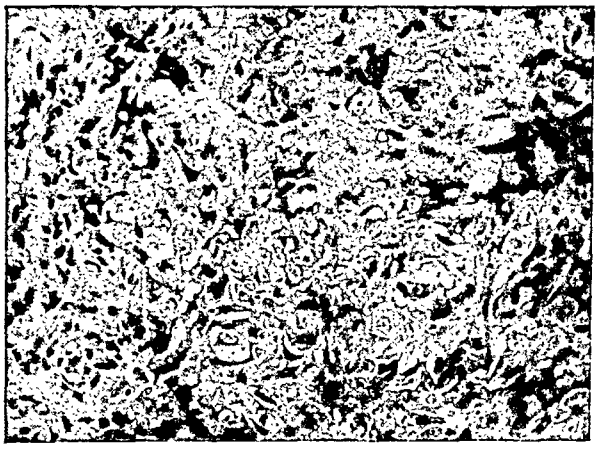


Fig. 5 Case ix. Section showing highly anaplastic carcinoma

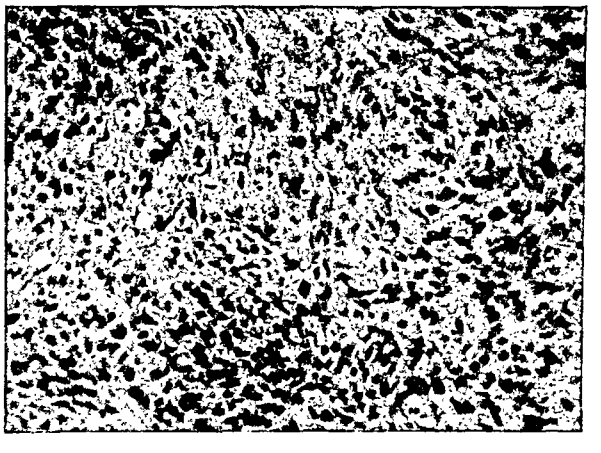


Fig. 6. Case ix. Section of same specimen showing an area strongly suggestive of sarcoma.

followed by deep roentgen therapy, and who survived without recurrence thirteen years and three and one-half years respectively.

One patient had incomplete removal of the tumor followed by intensive irradiation. She was followed without evidence of recurrence for four years and two months after therapy.

Three of the 6 advanced cases showed marked palliative effect and only one showed little response to radiation therapy.

Two cases were lost during the course of therapy and no evaluation of their response can be made.

Examination of all these cases has convinced us that radiation therapy is very important adjuvant in the treatment of these patients.

We feel that there is a very definite place for preoperative roentgen or radium therapy since many of the patients are diagnosed by dilatation and curettage before hysterectomy. This is certainly true in view of the high operative mortality reported in several series.[7,10] The debilitating effect of this rapidly necrosing tumor undoubtedly contributes to this mortality. Intrauterine radium would do much to improve the preoperative condition of those patients whose tumors are present in the uterine cavity. Preoperative roentgen therapy may be used for the same purpose if the uterine cavity is so filled with neoplasm that insertion of radium is impossible. Cases VI and VII illustrate the remarkable improvement in general condition that followed radiation therapy. Total hysterectomy should follow irradiation in six to eight weeks.

Postoperative high voltage radiation therapy is indicated in all cases. Small foci of neoplasm can easily be left behind despite apparently adequate surgery. We feel that irradiation will arrest these foci in some cases. There are several cases in the literature which were followed over long periods of time despite residua or recurrence after surgery. Case III is another example of this.

Radium and roentgen therapy have a definite place as a palliative measure in advanced cases. Several of this series of cases showed gratifying palliation with radiation therapy.

SUMMARY

Nine cases of sarcoma of the uterus are presented and their treatment discussed.

Three operable cases were treated by combined surgery and postoperative roentgen therapy. Two are still well thirteen and three and a half years respectively. One was followed for four years and two months without recurrence even though tumor was known to be left by surgery.

Six inoperable cases were treated by irradiation alone. Three of these had comfortable life prolonged by radiation therapy.

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Vol. 61, No. 6

STUDIES ON THE METABOLISM OF RADIOISOTOPES BY VARIOUS FUNGI AND BACTERIA

THE DISTRIBUTION OF ORGANISMS CONTAINING RADIOIODINE (I^{131}) IN THE ANIMAL BODY

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RADIOACTIVE iodine (I^{131}) has been used for some time in the study of thyroid physiology, and its distribution in tissues in relation to time of administration is well known.[1,3,7,9,10,15,16,23,24,25,27] It is known that certain thyroid carcinomas alter the iodine distribution.[5,8] This paper will deal with the apparently altered distribution of I^{131} when the solutions administered consist of spores or bacteria which have been grown in the presence of radioactive substance. The technique for raising "radioactive" fungi has been previously reported[21] but since then it has been rechecked and increased in scope.

MATERIALS AND METHODS

The radioactive I^{131} was received from the Atomic Energy Commission and was standardized immediately prior to use. A calculated dose was administered and in each experiment all of the radioactivity was finally accounted for.

The fungus cultures used in this study were from the stock culture supply of the Department of Bacteriology and were grown on Sabouraud's agar slants.

The cultures were checked grossly and also microscopically for spores and each culture tube was filled to the top of the agar slant with either sterile distilled water or physiological saline. These cultures were then taken to the isotope laboratory where the radioactive isotope was added to the clear solution (I^{131} 20–1,000 microcuries). During this transfer of radioactive iodine, two persons were involved and both used protective aprons and gloves. One person pipetted the calculated dose of I^{131} with proper equipment, while the other person handled the cultures with tongs. All equipment and personnel involved were checked for radioactive contamination upon completion of the transfers. The cultures were exposed to these solutions for forty-eight to 120 hours in the isotope laboratory.

After exposure, the cultures were taken to the bacteriology laboratory to be filtered. Here the cultures, Seitz filters to be used, and suction flasks were placed on a metal tray behind a protective shield, and all transfers and manipulations were made over the shield to prevent contaminating the laboratory with radioactive material or exposing the personnel. The person doing the filtering wore rubber gloves and apron and handled the test tubes with 12 inch tongs. Each culture was washed with sterile saline (three to five washings) until the filtrate was essentially radionegative. Each washing was collected in a 15 cc. centrifuge tube placed inside the suction flask and a Geiger count done on it. This tube also prevented contamination of the vacuum equipment by the radioactive solution.

When the filtrate was essentially radionegative, the material left upon the Seitz filter was tested for radioactivity; if positive, it was resuspended in saline and examined with a microscope to insure the presence of spores and mycelia. If this suspension was considered satisfactory, it was drawn into a sterile lead-protected 10 cc. syringe and injected intravenously into animals. Geiger counts were done on these animals thirty minutes after injection and daily thereafter.

Small amounts of the fungi remaining on the Seitz filter were smeared on microscope slides and checked with the Geiger counter for radioactivity. If considered sufficiently active to make a radioautograph, the slides were taken to a dark room and placed in contact with photographic plates for variable times, depending upon the amount of radioactivity (two to fourteen days).[5] An extremely fine grain photographic emulsion is necessary to record these small organisms. Kodak Nuclear Track plates,

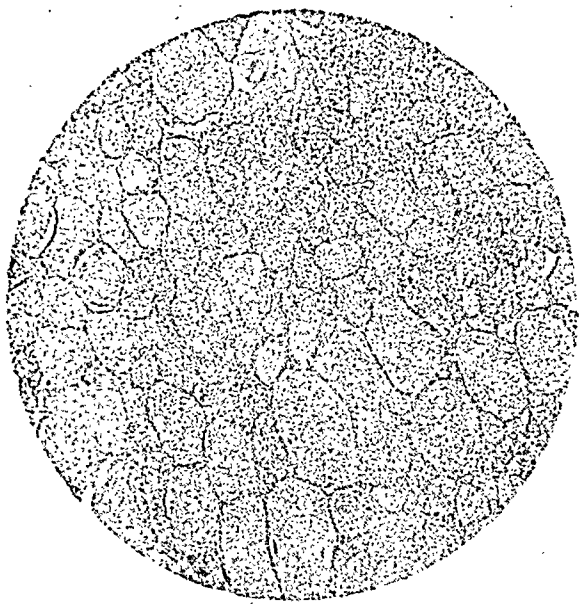


FIG. 1. Radioautograph of thyroid of a normal dog forty-eight hours after administration of 500 microcuries of I^{131} intravenously, showing the iodine distributed throughout the cells and colloid in a uniform manner. ×200. Hematoxylin and eosin stain on radioautograph.

Type NTB (25 Micron) were used.* These plates were then developed and the corresponding slide stained and both were examined microscopically.

* The authors wish to thank the Eastman Kodak Company who supplied the plates.

Pathogens (*Mycobacterium tuberculosis*, etc.) were handled essentially this way, except that the slide and film were kept in a petri dish which could be sterilized after completion of the radioautographs. As previously described, the pathogenic spore formers were always handled under a layer of liquid to prevent the dissemination of spores or radioactive particles into the air. The plates were developed in beakers which could also be sterilized after use.

RESULTS

Figure 1 shows a radioautograph of the thyroid of a normal dog made from animal 47–264. This animal received 500 microcuries of I^{131} intravenously forty-eight hours prior to a hemithyroidectomy. The technique used in preparing this specimen was that of Evans.[5]

Table 1 indicates by + signs the relative distribution of I^{131} in the various organs at the times that the animal was checked for radioactivity.

(1) It can be seen that, when various organisms have been exposed to I^{131} (animals 5–13), the iodine does not go directly to the thyroid gland as in the case of inorganic I^{131} solution (animals 1–4).

(2) If organisms are administered intravenously to the dog prior to exposure to

TABLE I

TABLE SHOWING THE RELATIVE DISTRIBUTION OF RADIOACTIVE IODINE FOLLOWING THE ADMINISTRATION OF STERILE INORGANIC I^{131} SOLUTION AND SUSPENSIONS OF MICRO-ORGANISMS WHICH HAVE BEEN MADE RADIOACTIVE

Dog No.		1*	2	3	4	5	6	7	8	9	10	11	12	13	14
1. (8–85) 16 lb. female brown chow, 100 microcuries I^{131}	T.**	1+	4+	4+	4+	3+	3+	2+							
	L.	3+	3+	1+	1+	1+	1+	±							
	S.	4+	3+	2+	1+	1+	1+	±							
	B.		±	±	±	o	o	o							
2. (47–264) 20 lb. female white mongrel, 500 microcuries I^{131}	T.		4+	4+											
	L.		2+	1+											
	S.		2+	1+											
	B.	4+	±	±											
3. (47–265) 19 lb. female brown mongrel, 1,000 microcuries I^{131}	T.		4+	4+											
	L.		2+	1+											
	S.		2+	1+											
	B.	4+	±	±											
4. (47–239) 20 lb. male black mongrel, 500 microcuries I^{131}	T.		4+	4+											
	L.		1+	1+											
	S.		1+	1+											
	B.	4+	±	±											

TABLE I—(*continued*)

Dog No.		1*	2	3	4	5	6	7	8	9	10	11	12	13	14
5. (47–78) 38 lb. female mongrel, *Alternaria* spores and I^{131}	T.	1+		1+			1+				1+				3+
	L.	3+		3+			2+				1+				o
	S.	3+		3+			3+				2+				o
	B.	1+		2+			1+				1+				o
6. (47–264, 48–5) 20 lb. male, white, long-haired, *Fusarium* and 20 microcuries I^{131}	T.	1+		3+							2+				
	L.	3+		1+							1+				
	S.	3+		o							1+				
	B.	1+		o							1+				
7. (48–5, 47–264) 18 lb. male, white, *Alternaria* and I^{131}	T.	3+	2+	2+	1+	1+	o	o							
	L.	4+	3+	4+	1+	±	o	o							
	S.	4+	2+	3+	1+	±	o	o							
	B.	2+	2+	1+	1+	±	o	o							
8. (48–85) 16 lb. female brown chow, *Alternaria* and I^{131}	T.	1+	1+	1+	±	±	±	2+	1+	o					
	L.	3+	3+	1+	3+	3+	3+	2+	±	o					
	S.	3+	1+	2+	3+	3+	3+	2+	1+	o					
	B.	1+	1+	1+	±	±	±	2+	1+	o					
9. (48–65) 15 lb. male bull, *Fusarium* and I^{131} (shock from *Fusarium*)	T.	o													
	L.	o													
	S.	o	o												
	B.														
10. (47–251) 20 lb. female brown chow, *Oospora* and I^{131}	T.	2+	1+	1+	±	1+	1+	o							
	L.	2+	1+	1+	o	o	o	o							
	S.	3+	1+	1+	o	1+	1+	o							
	B.	1+	1+	1+	o	o	o	o							
11. (47–147) 24 lb. female, black and brown terrier *Blastomyces, Actinomyces, Monilia, Histoplasma, Cryptococcus, Sporotrichium* and I^{131}	T.	1+		1+					1+						o
	L.	2+		2+					1+						o
	S.	2+		2+					2+						o
	B.	1+		1+					1+						o
12. (47–243) 30 lb. male, black hound, tubercle bacilli and I^{131}	T.	2+	2+	3+	1+	±	o	o							
	L.	1+	1+	1+	1+	1+	±	±							
	S.	1+	1+	1+	o	o	o	o							
	B.	1+	1+	1+	o	o	o	o							
13. (47–251) 20 lb. female brown chow, *Fusarium* intravenously, I^{131} intravenously, 20 microcuries	T.	4+			4+							4+			
	L.	2+			o							±			
	S.	2+			1+							±			
	B.	1+			o							±			
14. (00–000) 15 lb. male, black and white, *Fusarium* and 50 microcuries I^{131}	T.	2+	3+	4+											
	L.	3+	1+	—											
	S.	2+	1+	—											
	B.	2+	1+	—											

* 30–60 minutes.
** Thyroid, Liver, Spleen, Bladder.
± =doubtful.

I^{131} (animals 13–14) and inorganic I^{131} solution administered later, the iodine is distributed in the same manner as in the controls (1–4).

Animal 48–85 (8) was given *Alternaria* $+I^{131}$ and the iodine did not go to the thyroid directly. Several months later the same animal was given 100 microcuries I^{131} (1) which followed the expected iodine distribution.

Figures 2, 3 and 4 show radioautographs of microorganisms (see explanation of plates).

DISCUSSION

As we have shown in a previous publication,[21] all of the radioactive element present

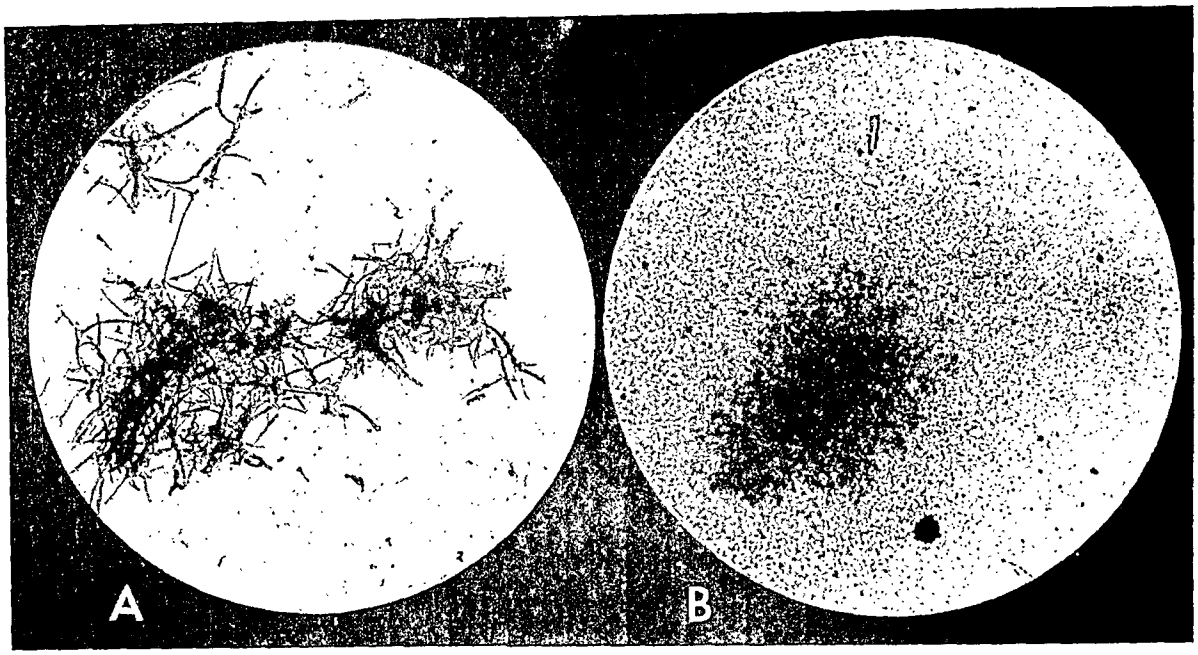


FIG. 2. *A*, *Fusarium* after a ninety-six hour exposure to 300 microcuries of I^{131}. Dilute methylene blue stain. ×200. *B*, radioautograph of *A*.

in the suspensions of organisms which were injected into animals had been actually metabolized by and incorporated into the organisms. The concentrations of pure organisms on the filters were leached and washed until the washings gave less than 10 counts per minute per milliliter above background. The organisms were then resuspended in fresh (non-radioactive) sterile saline. In subsequent radioautographs, the organisms proved to be very active, while neither the dried suspension medium nor fibers from the Seitz filters showed any detectable activity.

Animals 1–4 are the control animals that received dosages of 100 to 1,000 microcuries of I^{131} intravenously. These animals revealed large accumulations of I^{131} in the

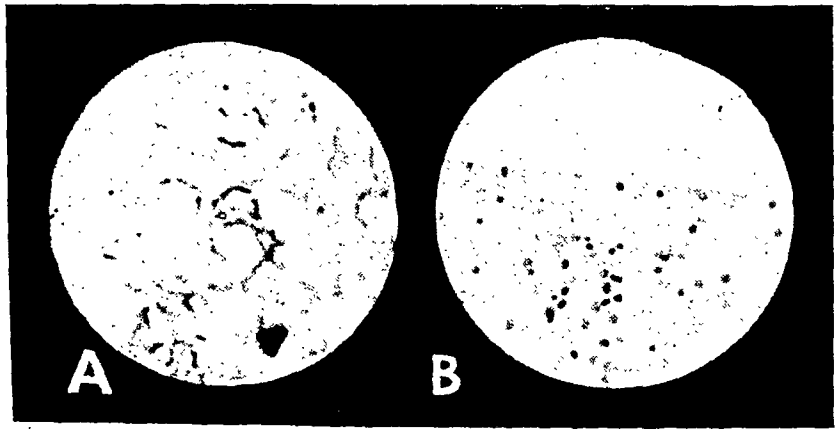


FIG. 3. *A*, *Mycobacterium tuberculosis* after a ninety-six hour exposure to 300 microcuries of I^{131}. Ziehl-Nielsen stain. ×1250. *B*, radioautograph of *A* on Eastman NTB 25 micron uncoated plate. ×1250. The radioautographs demonstrated that the isotope was present in the organisms in sufficient quantity to affect the plate. At the magnification used the depth of focus was decreased to the extent that all of the affected silver granules could not be focused in the same plane, therefore these radioautographs are not as satisfactory as those done on colonies at lower magnifications.

region of the bladder immediately (thirty to sixty minutes) after the injection and most of the I^{131} in the thyroid area at the twenty-four hour period and thereafter. This is the expected or predicted distribution of the I^{131}.

In animals 5–12 inclusive the radioactive iodine, which was taken up by the various fungi (pathogens and non-pathogens) and tubercle bacilli prior to injection, did not follow the same distribution as uncombined inorganic I^{131}. Instead of going to the thyroid as in the controls, the iodine apparently remained within the micro-organisms, which were picked up by the reticulo-endothelial system, until these were destroyed.

Alternaria containing I^{131} was injected intravenously into animal 5 and, as shown in Table 1, did not go directly to the thyroid. The animal was sacrificed in fourteen days and Geiger counts on the viscera showed radioactivity in the thyroid only. Cultures from liver, spleen and lung failed to show evidence of the injected organism. Apparently, when the *Alternaria* was destroyed by the macrophages in the liver and spleen, the iodine was released and then went to the thyroid gland.

The ability of fungi to absorb and to retain the radioiodine varies with the genera; therefore, it was not always possible to give the same quantity of radioactivity in a tolerable quantity of suspension of the organism. The quantitative uptake and retention of radioactive isotopes by micro-organisms has been the subject of a previous publication and this study is being continued. For the purposes of this paper, the quantitative value of the dosage is not significant since our purpose was to study: (1) the initial localization of the radioactivity, (2) its subsequent distribution and (3) its final disposition in the animal body.

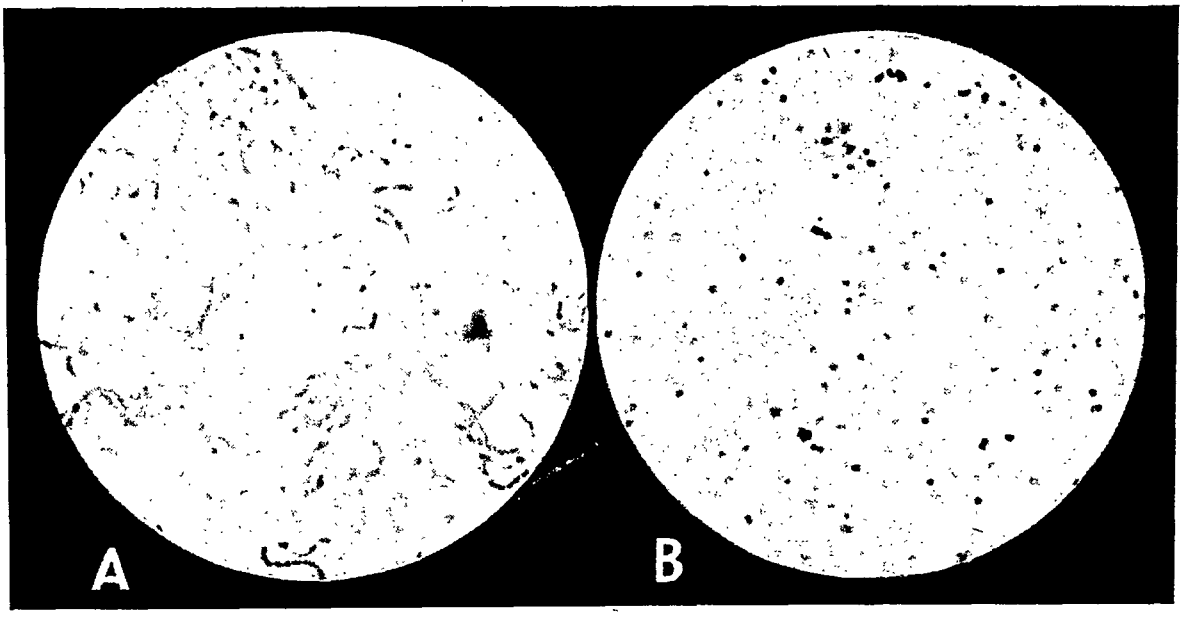


FIG. 4. *A* and *B*, same as Figure 3 except ×1500.

For example, animal 6 and 7 are the same dog employed twice in two different experiments to contrast the rates of exchange of radioiodine in the case of *Fusarium* and of *Alternaria*. As No. 6, this animal was injected with *Fusarium* containing I^{131}. Nine months later this same animal was injected with *Alternaria* prepared in the same manner. As will be seen from Table 1, the *Alternaria* retained the radioactive tracer in the liver and spleen for a much longer period of time than did the *Fusarium*, although both caused its retention in these organs much longer (days)

than the normal retention period for simple inorganic radioiodine, as shown in the control animals.

In animal 8 the *Alternaria*-radioiodine study was repeated in a different animal and the results in animal 7 were confirmed.

The technique of injecting significant quantities of suspensions of the micro-organisms constituted a problem in itself, particularly when a high specific radioactivity within the organism made standard procedures of colloid preparation impractical or difficult. In general, it was demonstrated that 5 milliliters of a suspension of micro-organisms having just a faintly opalescent appearance and containing about 5 milligrams of organisms per milliliter was the maximum which could be administered safely.

Animal 9 was the only one killed unintentionally. In this case a suspension of *Fusarium* mycelium, which had been cleared as completely as possible of spores, was injected. It was not found possible to reduce the particle size of this suspension to a desirable level and visible small clusters were present. This animal went into shock and died immediately. Multiple emboli were found in the lungs at autopsy. It was demonstrated that the clusters of mycelia had served as nuclei for the emboli.

In animal 10 *Oospora* containing I^{131} was injected and the resulting iodine uptake was demonstrated to be altered in a manner similar to that in the case of *Alternaria*.

In animal 11 *Blastomyces dermatitidis* containing I^{131} was injected intravenously. Geiger counter examination revealed altered I^{131} distribution, the activity being found in the chest, liver and splenic areas. This animal died at the end of twenty-one days of systemic blastomycosis as proved by cultures of lung, liver, spleen and nasal secretion and by microscopic sections. Splenic aspirations on this animal during life were positive for *Blastomyces* on culture and were radioactive for a period of eight days. After fourteen days there was no detectable radioactivity in any area. Cultures for organisms other than *Blastomyces* were negative throughout. At no time during this experiment was a significant concentration of radioiodine built up in the thyroid.

A partial study was also conducted with *Actinomyces asteroides*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Candida albicans* and *Sporotrichum schenckii*. Only one experiment could be conducted with these organisms and, hence, the results are not considered conclusive. There was no indication that the behavior of the radioiodine present in these organisms gave any result different from that described with the *Blastomyces*.

In contrast to the non-pathogens, the *Blastomyces* was not destroyed by the reticulo-endothelial system, but continued to multiply and eventually killed the host. It is demonstrated by this experiment that the pathogen alters the iodine distribution in a manner different from the non-pathogen in that no significant concentration of radioiodine is released to be collected in the thyroid.

In animal 12 *Mycobacterium tuberculosis* (human) containing I^{131} was administered intravenously. Radioiodine appeared quickly in the thyroid but in weak concentration, representing about 10 per cent of the dose administered. This probably represents some actual destruction of the organism or an attack upon its waxy capsule, since the preparation had been washed clean of radioactivity before administration. After the third day there was a decrease in the activity of the thyroid to a negligible level but a continued, significant radioactivity was demonstrable in the liver area. This animal was sacrificed and found to have a miliary tuberculosis involving the lungs, liver, spleen and tracheobronchial lymph nodes. The organism was recovered on postmortem culture of all of the above organs. The significance of this experiment lies in the fact that it was demonstrated that the radioactive tracer was retained in the area most affected by the tuberculosis infection. These results may, in part, explain the fact demonstrated re-

peatedly in this laboratory, that tuberculous lesions simulate in some respects the iodine metabolism of aberrant thyroid tissue in the human. In any case, it demonstrates a practical technique for tracing the path of these organisms.

Many check experiments were performed in order to be sure that the results presented were not due to some factor other than those to which they are ascribed. For example, animal 13 was given *Fusarium* intravenously one week prior to injection of I^{131}. A standard tracer dose of radioiodine was administered at the end of the week and was found to follow the standard pattern for a normal animal without any demonstrable abnormality. It is illustrated that neither the non-pathogenic *Fusarium* nor any minor lesions which it may have produced due to mechanical obstruction or other possible side effect influenced the course of the radioactive tracer. Since it might not be expected that active *Fusarium* would still be present to any significant extent in the animal body at the end of one week, this experiment was repeated with a suspension of *Fusarium* administered fifteen minutes before the administration of 100 microcuries of radioactive iodine. Geiger counter studies were started at the end of an additional ten minutes and continued throughout the next thirty minutes. Serial studies were conducted in the usual manner thereafter.

In Table 1 only one entry is made representing the first day; this is the average count of the first day. By the second day there was only the normal distribution of radioactivity in the liver and spleen which gave 550 and 560 counts per minute respectively compared to 1,450 for the thyroid. On the third day the thyroid count was 1,800 counts per minute, while the spleen gave 150 and the liver 130. The soft tissue showed a normal rate of decrease throughout. There was no excess of activity over the site of injection and counts over both shoulders were identical. It was demonstrated that the injection of *Fusarium* had absolutely no effect upon the distribution of the radioactive iodine injected into the same vein fifteen minutes later.

CONCLUSIONS

1. The distribution of pathogenic and non-pathogenic organisms administered intravenously can be followed by first making the organism radioactive.
2. Relative rates of destruction of non-pathogens are demonstrated by the decrease in radioactivity of the reticuloendothelial system and increase in radioactivity of the thyroid when I^{131} is used as the tracer.
3. The relative indestructibility of the pathogens as compared to the non-pathogens is illustrated by the retention of the radioactive tracer in the lesions of blastomycosis and tuberculosis.
4. Various techniques, including radioautographs, for the study of these effects are presented.

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DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

PORTABLE PROJECTOR FOR ROENTGENOGRAMS*

By RAYMOND A. DILLON, M.D., *and* WILLIAM P. MURPHY, JR., M.D.
BOSTON, MASSACHUSETTS

THE authors have long felt that some type of apparatus to project full sized, original roentgenograms on to a large screen would be of utmost value wherever roentgenograms are to be demonstrated. For some time one of us has attempted to show roentgenograms to large groups at hospital staff meetings, roentgenologic conferences, professional societies and to classes of medical students. Conventional methods have left much to be desired. All but the grossest detail on the film is lost to those beyond the first few rows.

The use of the view box, with all of its recent improvements, is obviously unsatisfactory both to the audience and to the speaker. Often the field under discussion cannot be seen satisfactorily even with a pair of binoculars. Reproducing films on a lantern slide not only entails much delay and expense, but the result is often disappointing. This is partially due to the photographer not knowing what range of tones to reproduce, and to the physical impossibility of reproducing on a single-coated emulsion the full scale of tones present on a properly exposed double-coated roentgen film.

After much thought over a period of years, and experimentation with numerous methods of projection, the present apparatus was constructed. Numerous light sources were tried and many condenser



FIG. 1. The roentgenogram to be demonstrated is placed on the field condenser. The small section on the right contains the light source, cooling equipment and preliminary condensers. A 45 degree mirror in the large section directs a horizontal beam up through the field lenses and film. The light is converged on to the overhead projection lens and is reflected to the screen by a surface-coated mirror. The height of the overhead projecting system is such that a person walking in front of the apparatus will not interfere with the image on the screen.

* Shown in an exhibit at the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept 14–17, 1948.

systems were investigated. A major obstacle has always been the unavailability of commercially made components. After the present optical system was decided upon, most of the lenses had to be individually designed and ground. Plastic lenses have proved unsatisfactory.

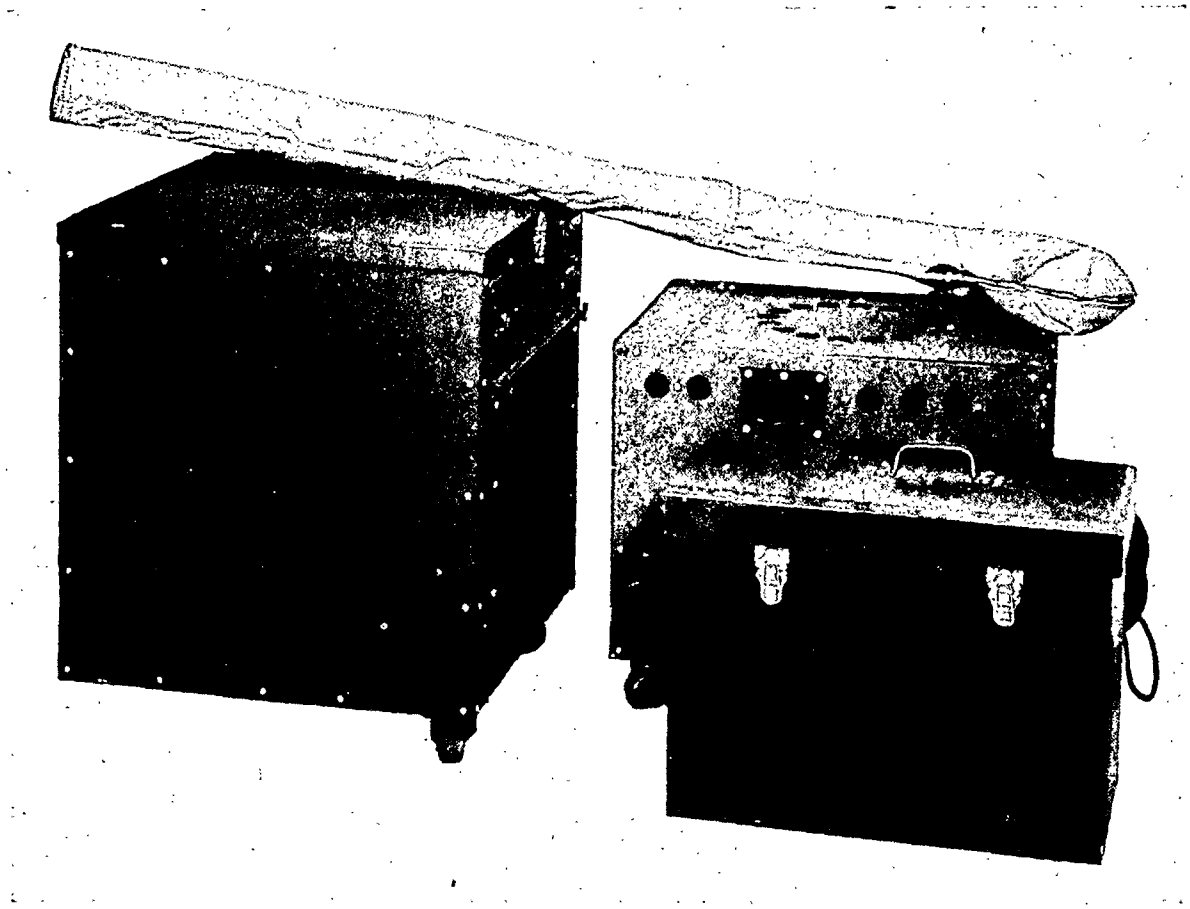


Fig. 2. In spite of the weight and size, the equipment is relatively easy to transport because it readily separates into four main components. When taken apart, metal doors are arranged to fit over the openings and protect the various lenses. Rubber wheels allow the individual sections to be rolled along the floor, or the whole apparatus assembled can be pushed from room to room. Disappearing handles allow the sections to be easily carried.

Because of the large size of a 14 by 17 inch film, as compared with a 35 mm. or standard lantern slide, this type of projector must, of necessity, have large physical dimensions. Some of the lenses weigh seventy pounds each. To save weight, many of the mounts, and other metal parts, are cast aluminum.

In spite of the weight and size, the equipment is relatively easy to transport because it readily separates into four main components. When taken apart, metal doors are arranged to fit over the openings and protect the various lenses. Rubber wheels allow the individual sections to be rolled along the floor, or the whole apparatus assembled can be pushed from room to room. Disappearing handles allow the sections to be easily carried.

The smaller section contains the light source, cooling equipment and preliminary condensers. These are mounted in a vertical position. The larger section contains the field condenser system which is mounted horizontally. It is protected by a piece of plate glass directly above, on which the film to be projected is placed. In this section

is a mirror placed at 45 degrees to the optical axis which serves to redirect the horizontal beam up through the field lenses. The light beam, having passed through the field condenser and the film, now converges to pass through the projection lens mounted in the overarm. It is reflected toward the screen by a second surface-coated mirror.

The instrument may be placed in any upright position relative to the screen. The overhead reflecting mirror can be tilted up or down, as well as turned through 360 degrees. A sharp focus is obtained by racking the projecting lens up and down. The projecting lens is a specially designed achromat of large numerical aperture. Due to the large size of the image to be projected, great difficulty was encountered in designing lenses to provide a sharp focus throughout the field, but this was finally accomplished.

Since the apparatus was meant to be used in many different institutions, the entire source and cooling equipment were constructed so that they could be supplied from the average electrical outlet and not require special wiring or special kinds, or amounts, of electricity.

In use, the film to be demonstrated is simply placed on the field condenser aperture and the electricity switched on. At a distance of 30 feet, the image fills a 6 by 8 foot screen. Separate case roentgenograms are easily shown and the entire teaching collection of a department is made immediately available for routine demonstrations. No detail is lost in projection for the original film is used as the image. Multiple films, such as sinus views or spot films, may be shown simultaneously. For example, four 5 inch diameter views may be projected at once. The lecturer may point out detail on the film and a clear image of the pointer used will be transmitted to the screen. Marks made on the film will be clearly shown. Cleared film or white paper may be used for diagram and any drawings or writing, such as one would make on a blackboard, will be seen greatly magnified. Photographs may be enlarged on roentgen-ray film and likewise projected.

The greatest problem in projection of roentgenograms has always been the tremendous amount of heat produced by the light source and transmitted to the film. Using any one of the innumerable possible projection methods, it is an easy matter to obtain almost any amount of light on the screen simply by increasing the amount of light at the source, but the film is likely to catch on fire. The great difficulty is that there is no efficient method of changing electrical energy into visible light. The best commercial projection bulb is less than 20 per cent efficient. This means that about 80 per cent of the electrical energy is turned into heat and transmitted with the light. This projector uses a 1,500 watt bulb and thus there is produced about the same amount of heat as two hot plates on an electric stove. This great amount of heat is effectively separated from the visible light by differential reflection and absorption so that a film may be left on the machine indefinitely without damage of any kind.

During the past year, the apparatus has been used with many different groups, large and small, and in a variety of rooms and auditoriums; both day and night and with an assortment of screens. Brilliance and detail have been most satisfactory.

180 Marlborough St.
Boston, Mass.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Thirty-first Annual Meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

EDITORIALS

INTUSSUSCEPTION

THE function of the radiologist in the care of infants suspected of having intussusception may be considered in both its diagnostic and therapeutic aspects.

It has been stated that clinical diagnosis of intussusception in infants is usually simple with the recognition of colicky abdominal pain, palpation of an abdominal mass, and the observation of blood in the stools. Ladd and Gross,[1] in their authoritative text, report that the roentgen examination was resorted to in only 25 of 484 cases, or in about 5 per cent of the cases of intussusception observed at the Boston Children's Hospital. There is general agreement that the most important factor in a successful outcome of these cases is early diagnosis and treatment. It is evident that the earlier the diagnosis is to be made, the less characteristic the symptoms will be. Colicky abdominal pain is not always easy to recognize in infants and may be seen in a variety of conditions. Likewise, abdominal masses are difficult to palpate in a distressed infant and different observers may report differing impressions. Bleeding would seem to be a rather late manifestation when the intussusception has been present for some time and considerable vascular congestion has already developed. Signs of bowel obstruction are an even later manifestation and when this has occurred the bowel is often gangrenous and the intussusception irreducible. Mistakes in diagnosis are made and the procedure of exploratory laparotomy before other methods of investigation have been exhausted is to be deplored and is fortunately falling into disuse in recent years. The roentgen examination of the colon by barium enema provides a rapid, simple, accurate and reliable means of diagnosis in ileocolic intussusception, which is by far the most common type of intussusception in infants. If an early and accurate diagnosis is to be made it would seem that this procedure should be much more frequently employed.

The treatment of intussusception in this country has been almost entirely surgical. Ladd and Gross mention non-operative methods only to condemn them as dangerous and unwarranted. However, observers have reported the spontaneous reduction of intussusception and reduction has apparently occurred under ether anesthesia. Reduction has also been noted not infrequently following a diagnostic barium enema. It is reasonable to suppose that if an intussusception is recognized early a reduction could easily be accomplished by a gentle retrograde pressure such as may be exerted by a barium enema. The use of enemas of various types in the treatment of intussusception has a long history antedating the use of surgery. The barium enema administered under roentgenoscopic control and controlled hydrostatic pressure is, of course, a great improvement over other forms of treatment by enema. This method has been widely employed abroad with apparent success. The monograph of Hans Hellmer[2] on "Intussusception in Children; Diagnosis and Therapy with Barium Enema" records the experience at the University Clinics in Lund, Sweden, with 162 cases of intussusception observed in a period of fourteen years. Reduction was accomplished by barium enema in 80 per cent of

[1] Ladd, W. E., and Gross, R. E. Abdominal Surgery of Infancy and Childhood. W. B. Saunders Company, Philadelphia, 1947.

[2] Hellmer, Hans. Intussusception in Children; Diagnosis and Therapy with Barium Enema. *Acta radiol.*, suppl. 65, 1948.

the cases. There were no deaths in these cases. Among the 30 cases where operation was necessary there were 9 deaths. Lindberg and Morales[3] have more recently reported the successful treatment by barium enema of acute early intussusception in 18 consecutive cases in infancy. They emphasize the importance of early diagnosis for the success of this form of treatment. All of their patients had symptoms of less than twelve hours' duration and in 14 the symptoms had been present for less than six hours. The recent report by Ravitch and McCune[4] from the surgical department of the Johns Hopkins Hospital will undoubtedly stimulate the non-operative treatment of intussusception in this country. As surgeons they favor treatment by barium enema and record data showing that the mortality and morbidity in intussuscpetion have been much reduced since the treatment has been primarily by barium enema. They report 33 cases treated primarily by barium enema with no deaths and in 24 of these, or 73 per cent, reduction was accomplished by the barium enema alone. They provide convincing answers to the objections commonly raised to this method of treatment. The time required for the barium enema is not prohibitive and should not cause a serious delay if operation proves to be necessary. The accuracy of diagnosis of complete reduction by barium enema is high but the possibility of the rare ileo-ileal intussusception must be kept in mind. Recurrence of the intussusception is apparently higher following reduction by barium enema (16.5 per cent according to Hellmer) than following surgery (2 per cent according to Ladd and Gross). As for the lesions which may be responsible for the intussusception (Meckel's diverticulum, intestinal polyp or other tumor, and duplication), these are rare (5 per cent in the series of Ladd and Gross) and are better dealt with at a later operation than at the time the intussusception is reduced. As for possible rupture of the bowel, Ravitch and McCune state that it may occur during the course of reduction whether by hydrostatic pressure or manual manipulation but is much less likely to occur during a barium enema "since less force is employed and that force is diffusely distributed."

If the intussusception has not been completely reduced by barium enema the surgeon's task will have been simplified as the manual reduction of an ileocecal intussusception is much simpler than the manual displacement of the small intestine from the distal colon requiring a wider exposure and a more time-consuming manipulation.

The treatment of intussusception offers a test and a challenge for the close cooperation and interdependence of the pediatrician, surgeon, and radiologist.

WILLIAM A. EVANS, JR., M.D.

[3] Lindberg, Gustaf, and Morales, Olallo. Treatment of acute intussusception by an enema of roentgenologic contrast medium. *Am. J. Dis. Child.*, March, 1949, 77, 303–309.

[4] Ravitch, M. M., and McCune, R. M. Reduction of intussusception by barium enema; clinical and experimental study. *Ann. Surg.*, 1948, *128*, 904–917.

THOMAS S. STEWART
1876–1949

DR. THOMAS S. STEWART, a member of the American Roentgen Ray Society since 1903 and one of the pioneers in roentgenology in Philadelphia, died on February 19, 1949, at the age of seventy-three. The following notice was written by Dr. George E. Pfahler for publication in the program of the Philadelphia Roentgen Ray Society:

IN MEMORIAM DR. THOMAS S. STEWART

"We have lost another distinguished pioneer in roentgenology. Dr. Thomas S. Stewart was one of six roentgenologists who met in Dr. Charles Lester Leonard's office and founded the Philadelphia Roentgen Ray Society in 1905. Dr. William S. Newcomet and I are the only two of these pioneers remaining.

" 'Tom Stewart' as we called him was born August 2, 1876, and died February 19, 1949, at the age of seventy-three. His death is attributed to a series of heart attacks, the first of which occurred New Year's Eve, 1948.

"He retired from radiology in 1928. He did, however, retain his membership in both the Philadelphia and American Roentgen Ray Societies until the time of his death. He was an active member of the Academy of Natural Sciences and was Curator of the Microscopic Section. He was also a Fellow of the Royal Microscopical Society of London, and a life member of the Historical Society of Pennsylvania, and a member of the Philadelphia County Medical Society, the Medical Club of Philadelphia, and of the American Medical Association.

"He had his preliminary training and experience in association with Dr. Leonard at the University of Pennsylvania Hospital. During the celebration of the 50th Anniversary of the discovery of the Roentgen Rays, he and I helped to collect some of the x-ray tubes and induction coils that were used in Philadelphia as early as 1896. In 1905, and for a number of years thereafter, the Philadelphia Roentgen Ray Society met serially at the offices of the six members, at which time we demonstrated to each other any new apparatus, new technique or new observations. It was really a close fellowship. Tom was loved by all of us and was well informed."

GEORGE E. PFAHLER, M.D.



PERCY JOSEPH DELANO
1899–1949

PERCY JOSEPH DELANO died suddenly on January 13, 1949. Death was due to severe burns accidentally sustained in his home.

Dr. Delano was born in Kewaunee, Illinois, September 21, 1899. He spent his boyhood in Kewaunee and during the first World War served in the enlisted ranks of the Army of the United States. He came to Chicago where he received his premedical education at Northwestern University and his M.D. degree from the University of Illinois in 1927.

Following graduation he interned at the

Cook County Hospital and later returned to that institution where he studied radiology under the late Dr. Maximilian J. Hubeny. He became Chief of the Department of Radiology at the West Suburban Hospital in Oak Park, Illinois.

Dr. Delano was very active professionally. He contributed numerous articles to the radiological literature. He was a diplomate of the American Board of Radiology; a member of the American Roentgen Ray Society, of the American College of Radiology, of the Radiological Society of North America and a Fellow of the Chicago Roentgen Society and of the American Medical Association. In addition to his professional activities he found time to write short stories which had been published in American and English magazines and to pursue his hobby, the violin and piano.

Dr. Delano will be remembered by his colleagues as a man who was extremely generous with his time and knowledge which he was always willing to share with the many who sought his advice.

Robert F. Stokes, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

AMERICAN RADIUM SOCIETY
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland Auditorium and Statler Hotel, Cleveland, Ohio, Dec. 4–9, 1949.

AMERICAN COLLEGE OF RADIOLOGY
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: Atlantic City, N. J., June 8–10, 1949.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

ARIZONA ASSOCIATION OF PATHOLOGISTS AND RADIOLOGISTS
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. Joseph Daversa, 603 Fourth Ave., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Hannan, Cleveland Clinic, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

HOUSTON X-RAY CLUB
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA X-RAY CLUB
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

LOUISVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

Nebraska Radiological Society
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

Northern California Radiological Club
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August.

Ohio State Radiological Society
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual Meeting: May 20 and 21, 1949, Bedford Springs Hotel, Bedford, Pa.

Philadelphia Roentgen Ray Society
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Queens Roentgen Ray Society
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

Radiological Section, District of Columbia Medical Society
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of New Jersey
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Ralph E. Alexander, 101 Medical Arts Bldg. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Shirley-Savoy Hotel, Denver, Colo. August 18, 19, 20, 1949.

St. Louis Society of Radiologists
Secretary, Dr. C. J. Nolan, 737 University Club Bldg., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

Section on Radiology, California Medical Association
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, February 3 and 4, 1950.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-RAY STUDY CLUB OF SAN FRANCISCO
Secretary, Dr. W. F. Reynolds, University of California Hospital, San Francisco. Meets from January to July, 1949, at Lane Hall, Stanford University Hospital, and from July to December 1949, at San Francisco Hospital.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGIA Y FISIOTERAPIA
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. E. M. Crawford, 1535 Sherbrooke St., West, Montreal 26, Que. Meetings January and June.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANCAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

AUSTRALIAN AND NEW ZEALAND ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. I. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

SOUTH AMERICA

SOCIEDAD ARGENTINA DE RADIOLOGIA
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

SOCIEDAD DE RADIOLOGICA, CANCEROLOGIA Y FISICA MEDICA DEL URUGUAY
Secretary, Dr. Arias Bellini.

CONTINENTAL EUROPE

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

CESKOSLOVENSKÁ SPOLEČNOST PRO RÖNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

WARSAW SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD.
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

MOSCOW ROENTGEN RAY SOCIETY
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

SOCIETA ITALIANA DI *RADIOLOGIA MEDICA*
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The Annual Mid-Summer Meeting of the Rocky Mountain Radiological Society will be held in Denver, Colorado, at the Shirley-Savoy Hotel on August 18, 19 and 20, 1949. As will be noted on the program, there is to be a symposium and conference on medical economics, particularly as they pertain to radiology. Also, there will be a symposium on the lesser circulation and on chest diseases, as well as a symposium on radioactive isotopes. Further information concerning the meeting may be obtained from the Secretary, Dr. Maurice D. Frazer, Lincoln, Nebraska. The following program has been arranged:

Thursday Morning, August 18, 1949

9:30–11:00 Registration.

11:00–12:00 "Symposium on Ethics of Economics in Radiological Practice," James P. Kerby, M.D., Salt Lake City, presiding.

12:30 Round Table Luncheon

"Discussion of Ethics and Economics," James P. Kerby, M.D., Salt Lake City, presiding.

Thursday Afternoon, August 18, 1949

2:00 Howard B. Hunt, M.D., Omaha, presiding.

President, Rocky Mountain Radiological Society.

Address of Welcome, President Colorado State Medical Society.

2:10 Paul R. Weeks, M.D., Denver, presiding.

"Pathology of Congenital Heart Disease," Harold D. Palmer, M.D., Denver.

2:45 "Angiocardiography," J. E. Miller, M.D., Dallas.

3:30 "Hypertension of the Pulmonary Circulation," C. Allen Good, M.D., Rochester Minnesota.

4:00 "The Auxiliary Heart," W. Walter Wasson, M.D., Denver.

4:45 "Discussion"—John B. Grow, M.D., Denver. Carl J. Josephson, M.D., Denver. Wm. B. Condon, M.D., Denver.

5:00 Executive Session.

Thursday Evening, August 18, 1949

8:00 Joint Meeting with the Medical Society of the City and County of Denver.

Frederick H. Good, M.D., Denver, President of the Medical Society of the City and County of Denver.

Guest Speakers

Paul C. Swenson, M.D., Philadelphia, "Problems in the Roentgen Examination of the Gastrointestinal Tract."

Charles L. Martin, M.D., Dallas, "The Treatment of Intra-Oral Cancer."

Friday Morning, August 19, 1949

9:00 Thomas B. Bond, M.D., Ft. Worth, presiding.

Vice President, Rocky Mountain Radiological Society.

"Double Contrast Study of the Colon," Robert D. Moreton, M.D., Temple, Texas.

9:20 "Lesions of the Small Intestine," C. Allen Good, M.D., Rochester, Minnesota.

9:50 "Bronchography in Carcinoma of the Lungs," John W. Walker, M.D., Kansas City.

10:10 "Discussion"—Ira H. Lockwood, M.D., Kansas City. John T. McGreer, M.D., Lincoln.

10:25 "Diagnostic X-ray Procedures at the Time of Labor," Paul C. Swenson, M.D., Philadelphia.

11:00 "Uterosalpingography in the Diagnosis and Treatment of Sterility," Charles L. Martin, M.D., Dallas.

11:45 "Discussion"—Kenneth D. A. Allen, M.D., Denver. Charles G. Freed, M.D. E. Stewart Taylor, M.D.

12:30 Round Table Luncheon

"Discussion of Diagnostic Problems," Wm. W. McCaw, M.D., Greely, Colorado, presiding.

Friday Afternoon, August 19, 1949

2:00 Kenneth D. A. Allen, M.D., presiding. President-Elect, Rocky Mountain Radiological Society.

"Characteristics, Instrumentation and Safe Handling of Radioisotopes in Medical Practice, Paul G. Aebersold, Ph.D., Oak Ridge, Tennessee.

2:45 "Application of Radiophosphorus in Radiological Practice," Capres S. Hatchett, Amarillo, Texas.

3:15 "Studies on the Genesis and Function of Neoplasms of the Thyroid with Modern Tools," R. W. Rawson, M.D., New York.

4:00 "The Treatment of Hyperthyroidism

by Radioiodine," Earl R. Miller, M.D., San Francisco.

4:45 "Discussion"—Thad P. Sears, M.D., Fort Logan, Colorado. Charles F. Ingersoll, M.D., Fort Logan, Colorado.

5:00 Executive Session.

Friday Evening, August 19, 1949

7:00 Social Hour.

7:30 Informal Banquet, Howard B. Hunt, M.D., presiding.

8:45 Address: "Illustrated Travelogue Through Scandinavia and Great Britain," Hamilton Berg, M.D., Bismarck, North Dakota.

Saturday Morning, August 20, 1949

9:00 Installation of Officers, Howard B. Hunt, M.D., presiding.

9:10 M. Lowry Allen, M.D., Salt Lake City, presiding, Vice President, Rocky Mountain Radiological Society.

"Epidermoid Carcinoma of the Bulbar Conjunctiva," Edward J. Meister, M.D., Denver.

9:30 "Radiotherapy in Brain Tumors," Galen M. Tice, Kansas City.

10:00 "Cerebral Angiography," Earl R. Miller, San Francisco.

10:30 "Discussion"—Ophthalmologist and Neurosurgeon.

10:45 "High Voltage Radiography," E. Dale Trout, Ph.D., Milwaukee.

11:00 "Short Distance Radiography," James W. Lewis, M.D., Colorado Springs.

11:15 "Relation of the Atomic Energy Program to Medical Practice and Research," Paul G. Aebersold, Ph.D., Oak Ridge, Tennessee.

11:35 "Some Newer Aspects of Cancer Research," R. W. Rawson, M.D.

11:55 "Discussion"

12:30 Round Table Discussion of Therapy Problems, A. M. Popma, Boise, Idaho, presiding.

Saturday Afternoon, August 20, 1949

4:00 Annual Picnic—Pine Gables Ranch.

THIRD INTER-AMERICAN CONGRESS OF RADIOLOGY

The Third Inter-American Congress of Radiology (Tercer Congreso Inter-americano de Radiologia) will take place in Santiago, Chile, November 11 to 17, 1949, inclusive. The meetings will take place in the University of Santiago and in Viña del Mar, a summer resort near the capital.

There will be a scientific program and exhibit of radiographic documents, technical-commercial exhibits.

The official topics of the Congress will be the following:

A. "Radiological Exploration of the Cardiovascular System with Opaque Material." This official relation should refer essentially to the radiological exploration of the heart and great blood vessels. Inclusion in the official presentation of the exploration of the peripheral vascular system will be optional.

B. "Diagnosis and Simple Radiological Exploration of the Skull." With the object of facilitating its consideration, this subject has been divided into three official presentations:

(1) a. Skull in general.
b. Sella turcica.
(2) c. Orbits.
d. Paranasal cavities.
(3) e. Temporal bone.

These official presentations should constitute a short exposition, read without introducing cases, being a résumé of the experience in that country.

Official Essayists and Collaborators may bring all the material they wish, preferably full-size originals, for exhibition in the Scientific Exhibits. In view of the nature of this subject, the Executive Committee requests that collaborations be fundamentally objective, and insists on the exhibit, making the verbal part as brief as possible.

C. "Radiation Treatment of Cancer of the Tongue."

D. "Radiation Treatment of Cancer of the Cervix."

Official presentations on these two subjects should comprise essentially the following parts:

1. Radiotherapy technique.
2. Immediate and subsequent reactions, and,
3. Case reports illustrating the clinical degree and the histological type of cancer.

For the above topics there will be assigned one major relator and one discussant, but there will be opportunity for a number of so-called "free papers" or topics of the authors' choice. We need volunteers

for the major papers and for the free papers. Scientific exhibits are also desirable.

The undersigned has full particulars as to the details of the exhibits and how they should be prepared. Those who propose exhibits will please communicate with the undersigned.

For demonstration of the radiographic material there has been arranged a permanent exhibition in the same location as the meeting to be held in Santiago.

In arranging the program, free time has been set apart for various functions of social and touristic order for the pleasure of the visitors.

About two hundred and fifty radiologists were enrolled in the Second Inter-American Congress of Radiology which took place in Havana, Cuba, in November, 1946, and it is hoped that an equally good attendance may be counted upon for the Santiago meeting.

While the trip may seem long, those who are pressed for time may make the trip by air; those with more time will find it enjoyable to travel by boat, part or all of the way. A round trip of South America makes a delightful journey; for instance, going down via the Atlantic coast, visiting Havana, San Juan, and the principal ports in Brazil, Uruguay and the Argentine, then across the Andes by train or by plane to Santiago, Chile. After the meeting one may return via the Pacific coast by steamer through the Panama Canal or by plane. If the traveler has time, most pleasant visits may be made in Guatemala, Yucatan and perhaps in the capital city of Mexico. Various modifications of these trips are available, so that the absence may be as long as a couple of months or as short as twenty-one days. Southern Chile is noted for its tourist attractions.

Travel arrangements may be made individually or by your nearest travel agent. The McGuire Travel Agency, 333 North Michigan Avenue, Chicago 1, Illinois, has been serving our committee very acceptably. The travel agency should make all room reservations, but no matter how one travels, it is requested that the undersigned, as regional secretary, be informed.

Adherents to the Congress should send in a check for twenty dollars which will entitle him to the Proceedings of the Congress whether or not he attends the meeting. One may be a member without attending.

Of course, passports will have to be arranged and the necessary visas obtained. The travel agency will be of much assistance in this regard. Inquiries may also be addressed to us.

James T. Case, M.D.
Regional Secretary for the
United States
55 East Washington Street
Chicago 2, Illinois

CANCER TEACHING DAYS

A Cancer Teaching Day was presented on May 25, 1949, at Albany, New York, under the auspices of the Medical Society of the County of Albany, Albany Medical College, Medical Society of the State of New York, Third District Branch of the Medical Society of the State of New York, and the New York State Department of Health, Bureau of Cancer Control. The following papers were given at the afternoon and evening sessions:

The Biological Differentiation of Malignant Tissue. Harry S. N. Greene, M.D., New Haven, Conn.

Cancer: The Problem of Early Diagnosis. 16 mm. color, sound movie.

Cancer in Childhood. Harold W. Dargeon, M.D., New York, N. Y.

The Diagnosis and Treatment of Sarcomas of the Soft Parts. George T. Pack, M.D., New York, N. Y.

A Cancer Teaching Day was also presented on May 25, 1949, at Binghamton, New York, under the auspices of the Medical Society of the County of Broome, Medical Society of the State of New York, Sixth District Branch of the Medical Society of the State of New York, Binghamton City Department of Health, New York State Department of Health, Bureau of Cancer Control. The following papers were given at the afternoon and evening sessions.

Cancer: The Problem of Early Diagnosis. 16 mm. color, sound movie.

The Significance of Enlarged Lymph Nodes. Henry D. Diamond, M.D., New York, N. Y.

Clinical and Roentgenographic Diagnosis of Oral Tumors. Harold A. Solomon, D.D.S., Buffalo, N. Y.

Gastric Cancer—Newer Diagnostic Methods. William A. Cooper, M.D., New York, N. Y.

The Significance and Management of Abnormal Vaginal Bleeding. Clyde L. Randall, M.D., Buffalo, N. Y.

SYMPOSIUM ON MODERN PHYSICS

A symposium consisting of thirty-two lectures on Modern Physics will be given at Oak Ridge, Tennessee, from August 22 to September 2, 1949, under the sponsorship of the Oak Ridge National Laboratory and the Oak Ridge Institute of Nuclear Studies.

The lecture staff will be drawn from among the well-known physicists who are expected to spend the summer at the Oak Ridge National Laboratory. Among these are: Professor S. M. Dancoff, University of Illinois; Professor J. G. Daunt, Ohio State University; Professor Eugene Feenberg, Washington University; Professor Hubert M. James, University of Illinois; Dr. Alvin M. Weinberg, Oak Ridge National Laboratory. Professor N. Kurti, of Oxford University, also will be a lecturer.

The lectures will include such topics as the current status of meson theory, the new quantum electrodynamics, recent progress in low temperature physics, declassified nuclear reactor theory, and classical nuclear physics. The lectures will be in the nature of a progress report to physicists in general rather than research reports to individuals within highly specialized fields.

In addition to the physics staffs in Oak Ridge, the lectures will be open without charge to physics department staff members and graduate students in physics in the South and elsewhere and to individuals in related fields. The series is being offered primarily for physicists from Southern universities but it is open to others insofar as facilities permit.

Additional information may be obtained from the University Relations Division of the Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tennessee.

COURSE ON ONCOLOGY

A Course on Oncology—New Aspects will be given at the University of California Medical School, the Medical Center, San Francisco, California, September 12, 13 and 14, 1949, the Officers of Instruction being from the University of California Medical School. The course is open only to graduates of medical schools approved by the Council on Medical Education and Hospitals of the American Medical Association. The fee for the course is $40.00, payable at the time of enrollment, either by check or money order made payable to *The Regents of the University of California*. Information concerning the course may be obtained by writing to Stacy R. Mettier, M.D., Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22, California.

RESEARCH FELLOWSHIPS—THE AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians announces that a limited number of Fellowships in Medicine will be available from July 1, 1950–June 30, 1951. These Fellowships are designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in Internal Medicine. Assurance must be provided that the applicant will be acceptable in the laboratory or clinic of his choice and that he will be provided with the facilities necessary for the proper pursuit of his work. The stipend will be from $2,200 to $3,200. Application forms will be supplied on request to The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., and must be submitted in duplicate not later than October 1, 1949. Announcement of awards will be made November, 1949.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

THE TREATMENT OF MALIGNANT DISEASE BY RADIUM AND X-RAYS: BEING A PRACTICE OF RADIOTHERAPY. By Ralston Paterson, M.C., M.D., F.R.C.S.E., D.M.R.E., F.F.R., Christie Hospital and Holt Radium Institute, Manchester, England. Cloth. Pp. 622, with numerous drawings, photographs, tables and roentgenograms. Baltimore: Williams and Wilkins Company, 1948.

Among the numerous recent publications on various phases of radiation therapy and radiation effects, radiologists and particularly radiotherapists will welcome this work by Dr. Paterson. Its more than six hundred pages contain a complete description of the basic principles underlying radiotherapy (both roentgen rays and radium), as well as a large section on specific applications to carcinoma and other malignant diseases involving various regions of the body. The plan of the book is not complicated. The discussion is given in straightforward, clear language, illustrated by numerous drawings, photographs and roentgenograms. It is really radiotherapeutic practice, setting forth the principles and practices of the Radium Institute in Manchester, England, which is now part of the Christie Cancer Hospital and the Holt Radium Institute. The detail of the text is sufficiently comprehensive without achieving encyclopedic proportions.

The author does not mean to imply that the methods and ideas which he presents are essentially the most desirable or the only methods. He realizes that there are many alternative, equally well-founded approaches to the various problems. Rather than a complete textbook or a summation of the present status of radiotherapy, the author prefers that his work be regarded as a statement of radiotherapeutic practice specialty, which has resulted from a reasonable combination of the various procedures which have been well tested. Many of the major issues are still in the balance such as the nature of the lethal effect of irradiation on normal and malignant cells; the factors determining radiosensitivity; the real influence of time and intensity factors, and the biological significance of wavelength.

The first three chapters of the book set forth the particular principles on which the Manchester methods are founded. No doubt there will be changes as the result of further research and experience. The author properly states that it is impossible today to make any justifiable distinction between roentgen therapy and radium therapy. The principles of the two modalities are identical, differing only in certain factors dependent upon the origin of the two forms of radiation.

The author has taken for granted that the reader will have a knowledge of the physics of radiation, and starts with gamma rays after they have left the needle or tube and the roentgen rays as a beam of radiation on the patient's side of the filter. The author calls attention to the fact that in this book he has not been so directly concerned with the curability or otherwise of cancer but rather with an evaluation of radiotherapy as a method of treatment.

In the opinion of the reviewer this work is remarkably well done. It seems that every radiotherapist would need a copy of the book.

JAMES T. CASE, M.D.

RADON: ITS TECHNIQUE AND USE. By W. A. Jennings, B.Sc., A. Inst. P., Physicist to the Royal Northern Hospital and Prince of Wales's General Hospital, Joint Radiotherapy Centre, and S. Russ, C.B.E., D.Sc., F.Inst.P., Formerly Physicist to the Middlesex Hospital, London. Cloth. Price, 18s. Pp. 222, with 12 pages of half-tones and 49 figures. London: John Murray, 1948.

As stated in the preface, this book has been written as a book of reference on the subject of radon. It consists of three parts.

Part I considers the disintegration series from radium to lead, the general properties of radon and a broad description of its use in medicine, biology and industry.

Part II is an exhaustive treatment of the extraction and purification process, followed by an excellent discussion on the problems encountered in a Radon Center designed primarily to supply the needs of an exacting clinic.

Part III covers tumor dosimetry in a concise

but adequate manner; medical considerations are very briefly dealt with in a chapter by Mr. T. A. Green.

The shortcomings of this book are few; its merits are many. Among the first are lack of better reference to other types of radon plants described in the literature, omission of discussion on the subject of radiation protection, and omission of bibliography to the chapter on medical considerations. Its merits are reflected in the clear exposition of the numerous problems encountered and the painstaking description of the techniques available for their solution.

Physicists and physicians concerned with the preparation and use of radon for clinical application will find this book very instructive and very valuable.

L. D. MARINELLI

STANDARDS FOR THE DIAGNOSIS AND TREATMENT OF CANCER. By The Cancer Committee of the Iowa State Medical Society. Second edition. Cardboard. Price, $1.00. Pp. 160. Athens Press, Iowa City, Iowa, 1948.

This publication in its first edition (1937) was among the first group of manuals to be published by various state medical societies. Because of the developments in the intervening eleven years, this revised edition has been issued. It is the aim of this compendium to make available, in a simple and concise form, for the use of physicians in general practice, what the authors believe to be the minimum standards of diagnosis and treatment of cancer. Because the clinical facts about the more common malignant growths are widely scattered throughout medical literature, this type of presentation in handbook style makes readily available the essential symptomatology, recognized methods of diagnosis and a survey of therapeutic procedures. After a brief dissertation on various general aspects of malignant diseases and on the importance of the family doctor in the cancer problem, the more common cancerous diseases are discussed in 32 sections varying from one to seven pages in length. The text of each section is concise and, in accord with the stated intention of the authors, the presentation is generally dogmatic in attitude. Within these limits, the discussion is adequate, informative and achieves the objective of the manual. An excellent feature is the clear separation of early signs and symptoms from late ones; this serves to emphasize again and again the importance of early diagnosis. It cannot be expected that the recommendations for treatment would meet with complete agreement by all the workers in the field. In general, they are sound although the implied suggestion that a simple mastectomy may be adequate surgery for an apparently early breast cancer would certainly not meet with general approval. Likewise most radiation therapists would not agree that irradiation of a cancer of the tonsil should be stopped as soon as the gross tumor has regressed. Another excellent feature is a bibliography (14 pages) of original articles and monographs which gives access to the voluminous literature on cancer.

ISADORE LAMPE, M.D.

THE THYROID AND ITS DISEASES. By J. H. Means, M.D., Jackson Professor of Clinical Medicine, Harvard University, and Chief of the Medical Services, Massachusetts General Hospital. Second edition. Cloth. Price, $12.00. Pp. 571, with 63 illustrations. Philadelphia: J. B. Lippincott Co., 1948.

This is the best available monograph dealing with diseases of the thyroid gland. It is comprehensive in its scope, and the material presented is based on the mature judgment of an author who has had a continuous and intense personal interest in this subject for many years. When the reviewer first went to Boston, in 1917, thirty-two years ago, James Howard Means, Jackson Professor of Medicine, Harvard University, the author of this volume, was actively engaged in a study of thyroid disorders at the Massachusetts General Hospital, and was sponsoring one of the first clinical laboratories for the determination of the basal metabolic rate, a procedure then in its infancy.

This volume, in 21 chapters and almost 600 pages, presents his views and opinions concerning all phases of the functions and maladies affecting the thyroid gland. In addition, chapters on "The Pathology and Tumors of the Thyroid" by R. W. Rawson and on "Surgery of the Thyroid" by Oliver Cope have been included.

The reviewer is not entirely in accord with all of the views expressed, but it is to be expected that in any field as extensive as thyroid diseases and one in which our knowledge is constantly advancing, there will be differences of opinion. For example, all observers are not in accord concerning the use of antithyroid drugs, one of the most important advances in this field in recent years. Dr. Means advocates a daily dose of propylthiouracil, the preparation of choice,

which varies from 75 to 300 milligrams, as a detoxifying medication. Furthermore, he appears to be uncertain as to the most advantageous time to institute iodine as an adjunct form of therapy. The reviewer believes that the dose of propylthiouracil is 100 milligrams, t.i.d., daily, and this should be continued until the basal metabolic rate is zero or less, and then reduced to 100 to 150 milligrams daily. Furthermore, it is my opinion that iodine in the form of 4 minims of Lugol's solution daily should be given from the very beginning of treatment.

It is the belief of Dr. Means that propylthiouracil will produce a remission in patients with Graves' disease which will continue as long as the drug is given without interruption. This is correct but the statement is incomplete. It has been demonstrated, for example, that after the drug has been given for as long a period as is necessary to maintain the basal metabolic rate within normal limits for ten months or more, the therapy may then be discontinued completely, and in an appreciable number of patients a long remission will follow. The preparation is, therefore, not only highly satisfactory as preoperative medication but it should also be given consideration as a form of medical treatment.

It does not appear that the author has placed sufficient emphasis upon the important differences between exophthalmic goiter and toxic adenoma. In the reviewer's opinion, they are separate diseases with some aspects in common, but with significant variations in their behavior. For example, patients with toxic adenoma are less susceptible to the action of iodine, cancer may develop as a complication, they are more readily cured surgically, serious eye complications do not appear, they less frequently develop "thyroid crises," spontaneous remissions are less frequently observed, and cardiac complications are more commonly present. References to these differences have not been entirely omitted from the discussion; they appear much more important, however, to one who has practiced medicine in an area where nodular goiter is commonly observed.

One of the debatable aspects of thyroid disease is the clinical significance of a solitary nontoxic adenoma. Widely divergent views have been expressed about the possibility of such a condition progressing to the state of malignancy. It is stated in this monograph (p. 453) that "during the past 3 years we have made it a practice to advise surgical intervention in all patients found to have single discrete nodules of the thyroid." In 199 specimens thus obtained 19 per cent had malignancy. There follows a discussion of the discrepancy between the high incidence of malignancy in surgically removed thyroid tissue as compared with the relatively low percentage of thyroid cancer observed at necropsy. The conclusion of the discussion is with the statement that "one wonders as to the accuracy of some of these histological diagnoses made on surgically removed material," a point which deserves careful consideration.

The volume contains a comprehensive bibliography bearing on thyroid disorders, and hence is exceedingly valuable as a source of references bearing on these topics. The reviewer would warmly urge that in all such monographs the references with the full title be placed at the bottom of the page on which they are cited, rather than at the end of each chapter, as they are in this volume. Furthermore, in searching for a reference by any particular author, a complete alphabetical bibliography at the end of the book is always a great convenience.

The reviewer does not wish to detract from the value of the publication by any of the criticisms which have been made. In general, the volume is made up of an exceedingly well written collection of information bearing on the subject. It should be consulted by every person desiring to obtain a comprehensive and fundamental knowledge of this field.

Cyrus C. Sturgis, M.D.

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

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INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Skeletal System

JONSSON, G.: Points regarding synovial fibrosarcoma 867
HUGHES, E. S. R.: Osgood-Schlatter's disease 867
CAVE, E. F.: Fractures of the tibial condyles involving the knee joint 868
VARGA, C., RICHTER, M. N., and DESANCTIS, A. G.: Systemic aleukemic reticuloendotheliosis (Letterer-Siwe disease) 868
KEMP, F. H., and WILSON, D. C.: Some factors in aetiology of osteochondritis of spine ... 868
WATKINS, W. W.: "Last-straw" factor in low back disability 869

Blood and Lymph System

BAZY, L., HUGUIER, J., REBOUL, H., LAUBRY, P., and AUBERT, J.: On some technical aspects of arteriography 869

General

PACK, G. T.: Prepubertal melanoma of skin 870
REILLY, W. A., and LINDSAY, S.: Gargoylism (lipochondrodystrophy) 870

ROENTGEN AND RADIUM THERAPY

EBERHARD, T. P.: Treatment of epitheliomas of the skin 871
DEWULF, L.: Treatment of epithelioma of the eyelids 872
JACOBSSON, F.: Treatment of keloids at Radiumhemmet 872
MANJUNATH RAI, K.: Treatment of leucoderma and the technique employed 872
LAWRENCE, J. H., DOBSON, R. L., LOW-BEER, B. V. A., and BROWN, B. R.: Chronic myelogenous leukemia 873
BOGART, F. B., and IMLER, A. E.: Giant-cell tumors of bone 873
DENIER, A.: Treatment of brucellosis by total teleroentgen therapy 873
WASSON, W. W., and GREENING, R.: Further observations with intravaginal roentgen therapy of cancer of the female pelvis 874
BOWING, H. H.: Intracavitary radium therapy for carcinoma of the uterine cervix 874
WATERMAN, G. W.: Interstitial radium therapy in carcinoma of the cervix 875
DEL REGATO, J. A.: Transvaginal roentgen therapy in carcinoma of the cervix 875
JENKINSON, E. L., PIRKEY, E. L., and HAMERNIK, J. F.: Five-year end-results in treatment of carcinoma of uterine cervix 875
ERNST, E. C.: Improved methods of intravaginal roentgen and radium therapy in carcinoma of the cervix 875
FRIEDENWALD, J. S., BUSCHKE, W., and MOSES, SYLVIA G.: Comparison of effects of mustard, ultraviolet and x-radiation, and colchicine on the cornea 875
GUZMAN, L.: Cancer of the prostate 876
PERRY, T.: Sarcoma of the uterus 876
NOLAN, J. F., and STANBRO, W.: Dosage calculations for various plans of intravaginal therapy 876
NEARY, G. J.: Physical aspects of intracavitary radium treatment of carcinoma of cervix uteri. Part III 877
SPEERT, H.: Late recurrence of cervical carcinoma following radiation therapy 877
BOWING, H. H., and FRICKE, R. E.: Late results of radium therapy for carcinoma of uterine cervix 878

RADIOISOTOPES

HENSHAW, P. S., RILEY, E. F., and STAPLETON, G. E.: Biologic effects of pile radiations .. 879
DOUGHERTY, E. C., and LAWRENCE, J. H.: Isotopes in clinical and experimental medicine 879
KNAUSS, H. P.: Slide rule calculations of radioactive decay 880
LISCO, H., FINKEL, MIRIAM P., and BRUES, A. M.: Carcinogenic properties of radioactive fission products and of plutonium .. 880
STANLEY, M. M., and ASTWOOD, E. B.: Accumulation of radioactive iodide by thyroid gland in normal and thyrotoxic subjects and effect of thiocyanate on its discharge. 881

MISCELLANEOUS

Best, A., and Stroud, L.: A method of x-ray reproduction of the negative x-ray film 881
Camp, J. D.: A grid-front cassette 881
Goldfeder, A.: Further studies on the relation between radiation effects, cell viability, and induced resistance to malignant growth 881
Clark, G. L.: Medical, biological and industrial applications of monochromatic radiography and microradiography 881
Prosser, C. L.: The clinical sequence of physiological effects of ionizing radiation in animals 882
Barclay, A. E.: Microarteriography 883
Loverdo, A.: On the use for radiological protection of gloves laden with thorium oxide 884
Barron, E. S. G., Bartlett, G. R., and Miller, Z. B.: Effect of nitrogen mustards on enzymes and tissue metabolism 884
Freed, J. H., and others: Effect of low dosage roentgen radiation on gonadotropic function of hypophysis of the mature and immature female albino rat 884
Holmes, B. E.: Inhibition of ribo- and thymonucleic acid synthesis in tumor tissue by irradiation with x-rays 885
Allen, J. G., and others: An anticoagulant in the blood of dogs with hemorrhagic tendency after total body exposure to roentgen rays 885
Bloom, W.: Histological changes following radiation exposures 885
Fredericq, J., and Chèvremont, M.: Histological and histochemical study of skin of guinea pigs treated with roentgen rays ... 886

ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

Jonsson, Gunnar. Points regarding synovial fibrosarcoma. *Acta radiol.*, 1948, *29*, 356–357.

The most important differences between synovialoma and synovial fibrosarcoma are the following:

1. Synovialomas contain endothelium-lined cavities, formations which are lacking in synovial fibrosarcomas.

2. Synovialomas often metastasize to the regional lymph nodes. Synovial fibrosarcomas do not. Both types of tumor, on the other hand, metastasize to the lungs and other distant organs.

3. Synovialomas are often highly radiosensitive while synovial fibrosarcomas are insignificantly so. In other respects there is a great resemblance between the two types of tumor even as regards prognosis. Synovialomas are considered to have a very poor prognosis. The prognosis of synovial fibrosarcomas appears to be somewhat better but even these tumors must be regarded as very serious.

Knutsson pointed out in his article the diagnostic importance of the fact that synovial fibrosarcomas often contain calcific deposits. Deposits of this kind do not occur in synovialoma or inflammation in the tendon sheaths, bursa or joint capsules. The deposits which are characteristic in appearance can be demonstrated roentgenographically and permit a correct diagnosis in most cases.—*Mary Frances Vastine.*

Hughes, E. S. R. Osgood-Schlatter's disease. *Surg., Gynec. & Obst.*, March, 1948, *86*, 323–328.

A knowledge of the normal anatomical and roentgenological features of the tibial tuberosity in the varying stages of its development is indispensable if the true nature of Osgood-Schlatter's disease is to be understood.

It seems that the pathological change in this condition is primarily within the ligamentum patellae rather than in the apophysis. The ossification at the site of insertion is readily accounted for by the partial tearing of the ligamentum from the bone.

This conception of Osgood-Schlatter's disease as a "tendinitis ossificans" is in full accordance with all the known facts. Trauma was believed by both Osgood and Schlatter to be the cause of the painful tuberosity and this opinion is now regarded as correct. The finding by some authors that the first roentgen sign of this disease is a thickening of the ligamentum patellae; the almost constant roentgenographic demonstration of opaque material within the ligament; the increase in density of this material in successive roentgenograms, all favor the view that Osgood-Schlatter's disease is of the same pathology as myositis ossifications which occurs in the muscle and tendinous fibers of the brachialis at the elbow.

With the great number of variations possible in the roentgen appearances of the normal tuberosity it is most hazardous to diagnose Osgood-Schlatter's disease from such appearances as increased densities, osteoporosis, partial separation, pitting, irregularities, and similar conditions. The appearance of fragmentation is a normal stage in the apophyseal development. Osgood-Schlatter's disease cannot be compared with osteochondritis of the hip where fragmentation is a roentgen sign of disease. The only definite abnormality of the apophysis observed here was the osteoporosis of the surface at the site of insertion of the ligamentum. This was observed clearly in only 5 cases and its presence is accounted for by a reactive hyperemia at the site of the injury.

It may be concluded that there is the strongest evidence in support of the belief that Osgood-Schlatter's disease is primarily an intraligamentous rather than an epiphyseal condition.—*Mary Frances Vastine, M.D.*

CAVE, EDWIN F. Fractures of the tibial condyles involving the knee joint. *Surg., Gynec. & Obst.*, March, 1948, *86*, 289–294.

Fractures involving the joints, especially weight-bearing joints, should be restored to normal anatomical relationship as accurately as possible, and if necessary, by surgical measures. This applies particularly to fractures of the tibial condyles involving the knee joint.

The commonest and also the fracture most difficult to handle involving the tibial condyles is the "bumper" or "fender" fracture which produces major damage to the lateral tibial table with or without damage to the external semilunar cartilage, the internal lateral ligament, and the cruciate ligaments.

Roentgen Studies. Roentgenograms of both knees should be taken in the same relative positions with anteroposterior, lateral and oblique views. If the injured knee is held in a position of flexion, the normal knee should be roentgenographed in the same position. Little knowledge is gained from the lateral views while the anteroposterior and oblique views will reveal the diagnosis. Because of the soft tissue swelling, more than the usual roentgen-ray penetration should be used to demonstrate the fracture lines.

Conclusions

1. Many fractures of the tibial condyles with more than a moderate degree of displacement should be treated by open reduction and internal fixation.

2. The surgeon undertaking such an operation must be well trained in meticulous joint surgery.

3. Preliminary manipulation and compression of many fractures of the lateral and medial tibial condyles may do harm to the joint surface of the tibia and make the subsequent open reduction more difficult.

4. Extensive comminuted fractures involving both tibial condyles may not be successfully reduced either by closed manipulation or open reduction.

These conclusions are based on a study of 98 cases of which 24 patients were treated by open reduction and internal fixation.—*Mary Frances Vastine, M.D.*

VARGA, CHARLES, RICHTER, MAURICE N., and DESANCTIS, ADOLPH G. Systemic aleukemic reticuloendotheliosis (Letterer-Siwe disease). *Am. J. Dis. Child.*, March, 1948, *75*, 376–384.

Three cases of systemic aleukemic nonlipid reticuloendotheliosis are reported. In the first case, the only change noted in roentgenograms of the long bones was moderate calcium deficiency in the cancellous portions. In the second, roentgenograms of the long bones revealed no abnormality. In the third, proliferative periosteal changes with numerous small areas of rarefaction were found in the skull and long bones. Two of the patients exhibited cutaneous manifestations not unlike infected eczema.

Roentgen therapy was not used in the treatment because, the authors state, it is not generally considered effective and, in addition, a depression of the functional acitivity of the reticuloendothelial system by irradiation with aggravation of existing infection has been noted.

A brief discussion of the relation of the condition to many better known diseases is included and difficulties in diagnosis and resistance to therapy are discussed.—*R. S. Bromer, M.D.*

KEMP, F. H., and WILSON, D. C. Some factors in the aetiology of osteochondritis of the spine. *Brit. J. Radiol.*, Oct., 1947, *20*, 410–417.

Two families in the laboring class in villages in England have been studied roentgenographically. The characteristic changes of osteochon-

dritis of the spine were found in many members of both families. In one family the parents both presented upper dorsal kyphosis with changes indicating healed osteochondritis. Children born when the family was in fair financial circumstances and obtaining a fairly good diet have normal spines. Of the children who grew up in less favorable times, several have the same type of upper dorsal scoliosis as the parents, and of these, several have changes of osteochondritis.

In the second family, the father has a lower dorsal scoliosis, and a pronounced lordosis. The family circumstances have always been poor, with some chronic minimal malnutrition. Some of the children show the same type of abnormal curvature as the father, and of these, some show osteochondritis.

The authors feel that this investigation indicates that osteochondritis develops from a combination of poor posture, which may be copied from the parents, and poor feeding. Healing takes place with improvement in the social circumstances. Although the water supply of both families contains a moderate amount of fluorine, it was not felt that there was conclusive evidence that this played a part.—*E. F. Lang, M.D.*

Watkins, W. Warner. The "last-straw" factor in low back disability. *Radiology*, Jan., 1947, *48*, 20–28.

The author reviews 100 cases of low back disability examined and evaluated by the Medical Advisory Board of the Industrial Commission of Arizona, over a nine year period. Of these 100 cases, 42 showed no visible bone or joint pathology, 33 showed definite bone or joint changes and 25 showed developmental anomaly with or without bone changes. Of the 42 cases without demonstrable roentgenologic evidence of pathology, 59.5 per cent were classified as having symptoms not attributable to injury. Of the 58 cases showing visible bone and joint changes or development anomalies, 33 cases exhibited arthritis of varying degrees.

This analysis was presented in defense of the conclusions reached by the Medical Advisory Board as a possible basis for comparison with similar ratings established by other boards. The author, a radiologist, discusses the factor of adaptation of the human body to certain disease processes, this adaptation at times being altered by sudden stresses, by processes which require unfamiliar use of certain body organs, and by the added factor of nervous exhaustion. He uses the classification of arthritis set up by the American Rheumatism Association. He feels that the chronic bone and joint changes found in the lower spine will fall into one of three groups: (1) bone changes from specific infection and neoplasm, (2) rheumatoid arthritis and (3) osteo-arthritis.

He states that pain practically always precedes the development of visible bone changes in rheumatoid arthritis but that the bone changes in osteo-arthritis precede the development of symptoms.

The question often raised in the evaluation of back injuries is the following: "When a man has a slowly developing arthritis of the spine which is being compensated for by adaptive changes in structure and mechanics, so that his working ability is not materially reduced, and some last-straw factor which would not cripple a normal back breaks this compensatory adaptation and results in disability, to what extent shall the disability be chargeable to the accident?" It is interesting that in this series of 100 cases of low-back disability, only one myelographic examination was carried out, and this demonstrated an extruded disc at the fourth lumbar interspace.

The author stresses the necessity for an intelligently directed and carefully supervised rehabilitation of workers having low-back disabilities. —*Robert C. Pendergrass, M.D.*

BLOOD AND LYMPH SYSTEM

Bazy, L., Huguier, J., Reboul, H., Laubry, P., and Aubert, J. Sur quelques aspects techniques de l'artériographie. (On some technical aspects of arteriography.) *Arch. d. mal. du coeur*, March-April, 1948, No. 3–4, pp. 97–112.

Five criteria are given for satisfactory arteriography, the most important ones being the innocuousness and the rate of injection of the opaque substance. Great care should be taken to render this rate as nearly equal to the speed of the circulation as possible, to prevent vascular dilatations or spasms. The authors criticize the previous methods of arteriography (where arterial circulation is partially or completely blocked).

The authors believe their method, which they call arteriography with free circulation, meets better the criteria. Several excellent arteriograms accompany the article. Their method

enables a kinetic study also. They use a very hypertonic solution of tenebryl 411 (680 mg. of I per 1 cc.) 100 to 110 per cent—10 to 15 cc.—which they inject into the artery very slowly under controlled pressure of about 1,000 to 1,400 grams. The authors consider that this very slow injection of a very opaque substance will prevent abrupt changes in intravascular pressure except in individuals with definite vasomotor instability. Since 1935 they have tried to eliminate such persons from arteriographic studies by two tests: (1) the reflex oculocardiac reaction, and (2) the intracutaneous reaction with adrenaline. Also they do not use arteriography in cases of hyperspasm (Raynaud's disease, ischemic syndrome of Volkman) unless the study is imperative in which case they are very cautious.

The intra-arterial pressure should be controlled every moment to avoid hypertension which is the most important danger. The authors have perfected an apparatus which enables them to measure this pressure during the injection giving thus an important margin of safety. A direct injection into the abdominal aorta gave a complete visualization of the lower extremities (serial arteriograms every five seconds).

After an extensive study of the various contrast substances for arteriography, the authors state that the ideal substance has yet to be found. At the present, they think that tenebryl 411 (an organic-iodine compound) is the best.—*J. N. Sarian, M.D.*

GENERAL

Pack, George T. Prepubertal melanoma of skin. (Editorial) *Surg., Gynec. & Obst.*, March, 1948, *86*, 374–375.

The groups of nevus cells constituting this congenitial tumor may be in evidence at birth. The coloration of these tumors, however, seems to develop after birth with exposure to light. Many of these tumors do not increase in dimension except proportionately with the rate of the growth of the child. Many of these nevi are not visible at all until after the onset of puberty. A child with a few scattered pigmented moles here and there may, in company with the endocrine changes attendant on the state of puberty, have the rather sudden development of numerous pigmented nevi over the skin of the face, trunk and extremities. It is assumed that these are not new-growths in the strict sense of the word but that the congenital misplacement of these cells may have been present but unrecognized until influenced by the hormonal factors so increased at this time. With the onset of puberty the nevi become much more darkly pigmented and have a tendency to become elevated.

There is one important type of pigmented nevus which bears such a close resemblance to malignant melanoma that it is not possible, clinically, to distinguish between the two. This nevus is found in children up to the age of puberty. Even though this tumor has structurally the conformation of the true melanoma it ordinarily does not behave as such until after puberty. The author's experience with more than 900 cases of malignant melanoma has been that none of these melanotic tumors of infancy and childhood has metastasized to regional lymph nodes although many of them have been labeled as malignant melanoma by extremely competent pathologists. He suggests that we adopt such a term as "prepubertal melanoma" to indicate the group of tumors which resemble malignant melanoma histopathologically but do not behave as such.

It would seem that the malignant melanoma in its derivation from the pigmented nevus is a tumor closely related to the endocrine system and markedly influenced by the activity of the endocrines, notably the gonads, the suprarenal cortex and the hypophysis. It is obvious that complete surgical removal of all dark deeply pigmented nevi in childhood is necessary. Their removal in infancy and childhood entails very minor surgical procedures without the hazards of recurrence.

In reviewing the end-results of the treatment of melanoma at the Memorial Hospital the number of five year survivals without recurrence (definitive cures) was only 50 per cent as good in the group of patients whose ages extended from puberty to twenty-five years as it was in the older age group.—*Mary Frances Vastine, M.D.*

Reilly, William Anthony, and Lindsay, Stuart. Gargoylism (lipochondrodystrophy). *Am. J. Dis. Child.*, April, 1948, *75*, 595–607.

In this report are described the clinical, laboratory and roentgenographic manifestations seen in 16 patients with gargoylism observed during a seventeen year period. On 8 of these 16 patients autopsy was performed.

Gargoylism is a disease involving most of the tissues of the body. The skeleton is greatly

altered and may be the earliest site of clinical manifestations. The disease is usually characterized by the following signs: typical facies (like a gargoyle), resembling that of cretinism; cloudy corneas; skeletal changes in both bone and cartilage; dwarfism; infantilism; thickening of the skin and periarticular structures limiting extension of joints; hepatosplenomegaly, and mental retardation. There is occasional familial recurrence, but no predilection as to sex or race has been noted.

Observations by Tuthill at the first autopsy of the condition which was reported indicated the storage in the brain of a lipid resembling cerebrophosphatide. Other later reports of autopsies did not confirm this, but later Strauss also contended that an excess of lipid was found in the involved tissues. After a thorough search of the literature, the authors found 107 case reports up to January, 1947. The appearance of clinical signs in infants as young as two months of age (kyphosis), the familial recurrence in 5 of 13 of the families in their study and the altered skeletal growth, they think, would indicate a hereditary defect of the germ plasm. Likewise, the storage phenomenon in the tissues, possibly of the carbohydrate type, could be regarded as a constitutional metabolic disorder. They feel that there is storage of some material in the parenchymal cells of the body. This material is not lipid in nature and may be a carbohydrate. In a later paper, they will report in detail the pathologic lesions observed in their autopsies.

The paper contains discussions of the etiologic aspects, signs and symptoms, laboratory data, roentgenographic findings, diagnosis, prognosis and treatment. In roentgengrams, the skull is usually dolichocephalic and the frontal areas overlie the orbits anteriorly to a considerable degree. The sella turcica is elongated and is shallow. The clinoid processes are often poorly developed and stand upright and are not eroded. The maxilla and, in many patients, the ascending mandibular rami are underdeveloped. There is forward protrusion of the mandible with an overbite of the lower incisor teeth.

The scapulas, in many patients, are widened. The ribs have narrow roots and broad bodies, with necks which appear distorted. The clavicles are distorted and wide. The superior halves of some of the vertebral bodies (between the 12th thoracic and the 2nd lumbar level) do not ossify at the same rate as the inferior halves, so that there is a steplike formation in the anterior surfaces of these bodies, resulting in the kyphosis so often noted clinically.

In the extremities the magnitude of the changes varies greatly but they are more pronounced in the upper than in the lower extremities, and the upper extremities are invariably affected. There is decided retardation of epiphyseal maturation, with abnormal configuration of the shafts and irregular cartilaginous proliferation at the epiphyses. The shafts are short and stubby and exhibit bizarre swellings in the central portions which taper toward the ends. Reilly and Lindsay regard this as a significant diagnostic sign. The head of the humerus is thick and often has a valgus angulation. The articular surfaces and the epiphyseal plates of the lower ends of the radius and ulna face inward. The metacarpal bones, the proximal portions of the metatarsal bones and the phalanges are broadened and shortened, and the first two phalangeal bones are pointed at their ends. Both acetabulums are shallow, and the ischia are disproportionately small in relation to the ilia. The femurs show a coxa valga angulation of the neck and a malformed, flat appearance of the head. The necks are broad. Invariably genu valgum is present. Occasionally, there is a fragmentation in the ossification process and the epiphyseal plates often have irregular outlines of ossification.

The differential diagnosis from Morquio's disease is discussed in the section on diagnosis. The authors question whether Morquio's disease is essentially the skeletal form of gargoylism as their roentgenologic appearances are so similar. To date, there have been few adequate descriptions of the pathologic features of Morquio's disease. In a biopsy report of Shelling, the changes in Morquio's disease in the bones were similar to the osseous lesions found by the authors in gargoylism.

In the treatment of the condition, endocrine products are of no great value. Symptomatic therapy is indicated even if given only as a placebo. Families should be warned that the disease not infrequently may recur in future offspring.—*R. S. Bromer, M.D.*

ROENTGEN AND RADIUM THERAPY

EBERHARD, THEODORE P. Treatment of epitheliomas of the skin. *Radiology*, November, 1947, *49*, 620–626.

The author gives a plan of treatment for basal, squamous, and basosquamous cell epi-

theliomas of the skin which disregards histology as a criterion for choice of method. Biopsy is always taken so that the lesion is definitely established as belonging to the epithelioma group. The method of treatment depends primarily on the size and location of the lesion, and secondarily upon the anticipated cosmetic result. The size and location will often determine the relative advantages of radium, roentgen radiation and surgery. Voltages used in roentgen treatment varied from 120 to 140 kv. Daily doses of 300 and 400 r were first used, but better cosmetic results were obtained with smaller initial doses. The first 1,600 r were then given at the rate of 200 r per day, the next 1,200 r at 300 r per day and the next 800 r at 400 r per day. The total doses were aimed at getting at least 300 tissue roentgens into the depth of the tumor.

Statistics are given regarding 492 patients treated in three years. At the end of a three-year follow-up period, 327 patients (66.4 per cent) were living free of disease and 89 (18.1 per cent) had died of other diseases. With Magnusson's correction factor, the cure rate is 83.3 per cent. No significant differences are observed in the results from the three types of treatment.—*J. Paul Bennett, M.D.*

DEWULF, L. Le traitement de l'epithelioma des paupieres. (Treatment of epithelioma of the eyelids.) *J. belge de radiol.*, May, 1947, *30*, 255–264.

The author reviewed 76 cases of epithelioma of the eyelids treated by contact roentgen therapy. He lists the indications and contraindications of this form of treatment, and states why this treatment is preferred over radium therapy. The indications are as follows:

1. Technically the method of application is easier.
2. The roentgen-ray beam can be directed in such a way that the eye will receive a minimum amount of radiation.
3. The treatment can be made while the patient is ambulatory.
4. Contact roentgen therapy by the fractional method gives an almost invisible cicatrix.—*Panagiotis S. Nemfakos, M.D.*

JACOBSSON, FOLKE. The treatment of keloids at Radiumhemmet. *Acta radiol.*, 1948, *29*, 251–267.

At Radiumhemmet 625 cases of keloids have been treated during 1921–1941. In 112 cases the keloid had earlier been excised surgically one or more times with subsequent recurrence. Five hundred and forty-nine cases were treated with radium, 24 with radium and roentgen rays and 25 exclusively with roentgen rays. The keloid was excised in 27 cases and then within ten days the scar was prophylactically irradiated. Total regression of the keloid was obtained in 73.6 per cent of cases, considerable regression in 14.4 per cent, evident in 9 per cent, slight regression in 1.9 per cent and the result was unsatisfactory in 1.1 per cent.

A keloid ought to be treated with radium before it is more than one year old because it then becomes less radiosensitive. The best results are obtained in keloids caused by mechanical injury or operation and the poorest in keloids in the sternal region and in cases with more than one keloid and different causes. In the latter cases irradiation should be given prophylactically to every significant lesion of the skin.

Since 1936, the author has used radium in applicators as advised by Strandqvist. The dose is calculated as the number of roentgens delivered in a 1 centimeter tissue layer. The dosage varies between 600 and 1,200 r. A dose of 900 r, for example, is delivered in two hours by an applicator containing ten needles (100 mg. radium) arranged in one row.

A careful dose must be given to keloids caused by burns. Skin tolerance is decreased in these keloids and there is risk of necrosis.

If there is no definite regression of the keloid after one to one and a half years and there are still pronounced symptoms such as itching and pain, a second treatment should be given. In most cases, however, one treatment will be sufficient.

In irradiating spontaneous keloids, especially those in the sternal region, a margin of at least 5 mm. of the surrounding apparently normal skin should be treated. Large keloids should be treated with roentgen irradiation because the dose will be more uniform than with a radium applicator.

The combination of operation and subsequent irradiation is not recommended, as a rule. Since the results of irradiation alone are usually as good, this method should be tried first.—*Mary Frances Vastine.*

MANJUNATH RAI, K. Treatment of leucoderma and the technique employed. *Indian J. Radiol.*, May, 1947, *2*, 45–50.

The author had treated 12 cases of leukoderma (using superficial roentgen therapy) with good results in all. The dosage used was not stated, but he thought that the late effects of irradiation to large areas could very possibly discourage its general use.

Ultraviolet ray therapy was then tried and a 90 per cent cure rate of those treated was obtained in 186 cases. The technique and basis of selection of cases are given in the article.—*R. Datzman, M.D.*

Lawrence, J. H., Dobson, R. L., Low-Beer, B. V. A., and Brown, B. R. Chronic myelogenous leukemia. *J.A.M.A.*, March 6, 1948, *136*, 672–677.

Since P^{32} emits beta rays whose half-value layer of tissue is about 2 mm., it was thought this would be an excellent way to give localized irradiation to the marrow.

Calculations revealed that 1 microcurie per gram of tissue will give a total of approximately 40 r of body irradiation in a twenty-four hour period.

The usual doses given were 1–2 millicuries one to two times weekly for four to eight weeks but doses equivalent to 40 millicuries intravenously over a period of seventy-two days have been given.

One hundred twenty-nine patients with chronic myelogenous leukemia were studied. With individual variations, they were given the approximate dosage listed above in an attempt to bring about clinical and hematologic improvement without damaging the normal cells.

It was noted that prophylactic or preventive treatment was ineffective. In this group ordinarily treatment was required on an average every six to nine months; occasionally one to two years elapsed however. Average length of life after onset was three to seven years.

No evidence of lengthening of the life expectancy was found. Possible advantages are the ease of providing a generalized irradiation and doing this without radiation sickness.—*R. Datzman, M.D.*

Bogart, Franklin B., and Imler, Allison E. Giant-cell tumors of bone. *Radiology*, October, 1947, *49*, 432–440.

Most giant cell tumors of bone are benign, but there is evidence to indicate that a few are either malignant from the outset or eventually become malignant. There are a number of variants of the true giant cell tumor which, for clinical purposes, are considered giant cell tumors and are so treated. A biopsy of the tumor should be done, and there are usually no contraindications to biopsy unless the lesion is surgically inaccessible. Where the tumor is proved to be of the malignant type, it should be treated surgically. If the lesion is accessible, it should be entirely removed.

Tumors which appear clinically, microscopically, and roentgenographically to be benign may be successfully treated by irradiation. It is recognized that where they can be readily approached, they can also be successfully treated by surgical removal. In most cases it is not necessary to combine surgery and irradiation. In structures such as the spine, it seems to be a disadvantage to use curettage, since the surgery may weaken the bone where the tumor is located in a weight-bearing area. Irradiation alone produces calcification, which lends support to the involved area and results in an earlier cure.

Many have observed that cases previously treated by curettement do not subsequently respond satisfactorily to roentgen therapy. Hence, lesions which have recurred following surgical removal are believed to be best handled by surgery if the proper surgical approach can be attained.

The authors do not believe that the roentgen dosage at present advocated for children—a series of approximately 100 to 200 r delivered to the tumor and repeated at intervals of one to three months for two to four series—will cause epiphyseal damage. In some cases they have used much larger doses where growing epiphyses were not involved, giving as high a tumor dose as 1,500 r, with a second series of half that amount two months later. Experience indicates that the smaller doses are adequate. The authors agree with the previously expressed opinion that where no damage results to the skin and soft tissues, no damage will result to the epiphyses.

Four cases are described in detail, 3 in the spine and 1 in the proximal end of the tibia. All showed a satisfactory response to treatment. Three were treated by irradiation alone, and one by combining surgery and irradiation.—*Paul R. Dirkse, M.D.*

Denier, Andre. Traitement de la fievre de malte par la teleoroentgenotherapie totale. (Treatment of brucellosis by total teleroent-

gen therapy.) *J. belge de radiol.*, May, 1947, *30*, 265–271.

The author presents 17 cases, and his observations concerning his investigations. All his cases were of several weeks' and sometimes months' duration. These cases had previously received all the therapeutic methods including vaccine, colloidal metals, and sulfa drugs.

All the patients had positive serological tests. Sweating and weight loss were constant. After the first roentgen treatment there was a fall of the temperature by the second day. The factors used were as follows: 30–40 r according to the body structure of the individual, filter 1 mm. copper plus 2 mm. aluminum, 340 kv., distance 2 m. 60 cm.; position: the patient was lying on a stretcher and irradiation was applied to the entire body. The author always treats first the anterior surface and after that the posterior surface. A second dose was repeated after eight days and sometimes a third dose was necessary but this was not the rule.—*Panagiotis S. Nemfakos, M.D.*

WASSON, W. WALTER, and GREENING, ROY. Further observations with intravaginal roentgen therapy of cancer of the female pelvis. *Radiology*, October, 1947, *49*, 452–461.

The authors state the purpose of this paper is to discuss, not the successes, but rather the failures of transvaginal roentgen therapy, and to offer certain procedures with the hope of better end results. They stress the necessity for careful diagnosis and for careful selection of the treatment of choice.

In the average case 2,500 r is delivered to the structures of the birth canal by external irradiation. Since 4,000 r within the tumor cells is probably the optimal amount, there remains 1,500 r to be delivered, either by radium or intravaginal roentgen therapy. For intravaginal roentgen therapy 140 or 200 kv. is used. Care must be exercised in placing the cones so as to avoid overlapping of the areas and the production of delayed reaction and lack of uniformity of irradiation about the pelvic structures.

If a large vaginal cone 3 or 3.5 cm. in diameter is used, the radiation will cover the transverse diameter of the pelvis, provided that three areas are given in the transverse diameter. If smaller cones are used there will be a space between the areas treated which will receive very little radiation. In such a case radium may be given within the uterus, and the intravaginal radiation should then be limited to the cervix and to the nodes along the outer pelvic wall. The author recommends intracavitary radium in all second, third and fourth stages to complement the external and intravaginal roentgen therapy, particularly when the intravaginal cone is not large enough to deliver an adequate uniform dose throughout the pelvic canal. Because of delayed reaction about the cervix and vaginal vault, it is recommended that if a tumor dose of 5,000 r is given in one series it should not be repeated, at least in that amount.

Intravaginal roentgen therapy is also suggested for residual tumors following operation upon the uterus and ovaries, or about the cecum, bladder and rectum.

Another technique is offered when the intracavitary radium application is desired. By using modified bladder retention catheter, the radium may be placed inside the catheter and inserted into the urinary bladder. The radium is then inflated to the desired extent, which may be recorded and controlled by a manometer. This gives greater depth and uniformity of dosage which has been sought for some time in the treatment of tumors of the bladder and other structures.—*Gordon J. Culver, M.D.*

BOWING, HARRY H. Intracavitary radium therapy for carcinoma of the uterine cervix. *Radiology*, October, 1947, *49*, 406–410.

A method of intracavitary radium therapy is presented. All applications are made with the patient in the knee chest position. Individualization of each patient is stressed. Roentgen therapy is started a few days before radium therapy is completed.

Results are presented. From 1919 through 1929 the percentage of three year cures steadily increased. This was attributed to several factors including (*a*) a satisfactory method of vaginal endoscopy facilitating placement of the applicator and gauze packing with minimal trauma, (*b*) observation of the vaginal field during the initial days of therapy to guide the selection of treatment, (*c*) better distribution of the radium applicators, (d) early recognition and treatment of potential and actual complications, such as bleeding and serious hemorrhage, localized inflammation, and necrosis of tissue.—*J. Maxey Dell, Jr., M.D.*

Waterman, George W. Interstitial radium therapy in carcinoma of the cervix. *Radiology*, October, 1947, *49*, 411–412.

A method is presented using parametrial radium element needles. In addition a platinum capsule of 20 mg. content that will deliver into the cervico-uterine canal approximately 3,300 milligram-hours over a period of seven days is used. Adaptability of this method to all types and conditions of cancer of the cervix is stated. In the last 198 cases their absolute five year survival rate was 38.9 per cent. The method of implanting the needles is described. Sepsis, fistula formation and intestinal injury have not been in excess of such complications reported by others using different methods.—*J. Maxey Dell, Jr., M.D.*

del Regato, J. A. Transvaginal roentgen therapy in carcinoma of the cervix. *Radiology*, October, 1947, *49*, 413–414.

The importance of external roentgen therapy is emphasized. External therapy should logically precede the internal phase of the treatment. A method of transvaginal roentgen therapy is presented. This has the advantage of completing the external irradiation without trauma to the healing tissues and without infectious complications which so often hamper the practice of intracavitary curietherapy.

A 42 per cent three year survival rate in 52 consecutive, unselected patients is reported.—*J. Maxey Dell, Jr., M.D.*

Jenkinson, E. L., Pirkey, E. L., and Hamernik, J. F. Five-year end-results in the treatment of carcinoma of the uterine cervix. *Radiology*, October, 1947, *49*, 415–418.

Seventy-five cases followed out of 98 cases showed a five year survival rate of 30.6 per cent. Their treatment methods used in this series are presented.—*J. Maxey Dell, Jr., M.D.*

Ernst, Edwin C. Improved methods of intravaginal roentgen and radium therapy in carcinoma of the cervix. *Radiology*, October, 1947, *49*, 425–428.

Two types of expanding colpostats for radium therapy in carcinoma of the cervix are described and illustrated. More accurate and uniform irradiation of the cervix, parametria and vaginal wall is claimed. Areas of tissue necrosis have not been observed in a single case. The instruments are stated to be very adaptable to the different forms of distant parametrial involvement and vaginal vault extension. A roentgenographic check of the position of the colpostat in 29 cases of moderately advanced cancer of the cervix did not disclose any displacement or shifting of the radium capsules. The ease of introduction facilitates the fractionation of radium treatment when desirable and reduces the amount of radiation exposure to the operator.

Translucent, plastic, intravaginal cones for roentgen therapy are described. These are stated to be adaptable to the various forms of vaginal canals.

Short auxiliary metallic cones of appropriate length are inserted into the plastic cones and the roentgen beam directed through the cone.

Final evaluation of the clinical effectiveness of these methods is deferred for later communications.—*J. Maxey Dell, Jr., M.D.*

Friedenwald, Jonas S., Buschke, Wilhelm, and Moses, Sylvia G. Comparison of the effects of mustard, ultraviolet and x-radiation, and colchicine on the cornea. *Bull. Johns Hopkins Hosp.*, Feb., 1948, *82*, 312–325.

Similarity between the tissue reactions to the mustards with those following roentgen-ray and ultraviolet irradiation has been noted. Colchicine has somewhat similar actions. These agents produce erythema, vesication and ulceration of the skin. Visceral lesions following systemic administration of the mustards are similar in nature to those produced by deep roentgen therapy. This experimental study shows the similarity and differences of action of these agents on the beef and rat corneas. The dosages and time factors as well as the methods of application are discussed. Inhibition of mitosis was caused. Inhibition by roentgen irradiation was prompt whereas inhibition by ultraviolet and mustard developed slowly. Inhibitions of equal duration were less complete with ultraviolet and mustard than with roentgen rays. Recovery from the inhibition followed similar curves in all, but excessive mitotic activity following recovery was noted with ultraviolet and mustard but not with roentgen rays. Colchicine did not inhibit the onset of mitosis but stopped the process in metaphase. Nuclear fragmentation of the corneal cells was produced by ultraviolet, mustard and colchicine but not by roentgen

rays. Loosening of the corneal epithelium was produced by all four agents. An increase in extractable non-protein nitrogen in the cornea was found after exposure to ultraviolet and mustard but not to colchicine. The correlation of these reactions above to each other as well as the difference in mechanisms of action involved is speculated upon. Various other influencing factors are also discussed.—*Jerome J. Wiesner, M.D.*

GUZMAN, LEONARDO. Cancer of the prostate. *Radiology*, August, 1947, *49*, 214–222.

This is a plea for radiation therapy of cancer of the prostate in addition to any surgery and endocrine therapy which may be used. The author recommends implantation of radium needles into the local tumor plus external irradiation of all tumor, testes, adrenals and pituitary. His experience with 25 patients so treated indicates that good palliation may be expected, and occasionally a patient will survive a very long time. The original paper should be consulted for technical details of the radiation therapy. (While the reviewer agrees that the pain of bone metastases may be controlled by roentgen therapy, and the local tumor inhibited by interstitial radium, there is no sound experimental or clinical data which indicate that normal androgen producing cells can be influenced by the amount of radiation therapy recommended in this paper.)—*Robert P. Barden, M.D.*

PERRY, T. Sarcoma of the uterus. *New England J. Med.*, June 3, 1948, *238*, 793–799.

Eighteen cases of sarcoma of the uterus seen in the last eighteen years at the Rhode Island Hospital are presented. Leiomyosarcomas were the commonest, varying from recurrent fibroids of low malignancy to anaplastic, rapidly disseminating tumors. Round cell or stromal cell endometrial malignancies made up another large group. Several pleomorphic mixed tumors, including 3 carcinosarcomas, were seen. An infant with sarcoma botryoides, an extremely malignant tumor of the cervical portio of infants, growing in characteristic grapelike masses, was studied. Several giant cell sarcomas, of uncertain cellular origin, were included in the series.

At operation, tumor spread was usually extensive. Survival for more than a few years without recurrence was limited to those few patients who had small localized tumors showing few metastases histopathologically. Eight patients received preoperative or postoperative radiation therapy, with important irradiation response in only 2 cases. The first was a seventy year old woman with a small carcinosarcoma which became completely necrotic after 2,450 mg-hr. of preoperative intrauterine radium, without recurrence after five years. In the second, a large carcinosarcoma showed extensive but incomplete necrosis after preoperative treatment with 2,190 r to each of three fields.

Of incidental interest is the observation that 2 of the mixed cell sarcomas developed in women who had had intrauterine radium for menopausal bleeding six and ten years previously.—*Henry P. Brean, M.D.*

NOLAN, JAMES F., and STANBRO, WILLIAM. Dosage calculations for various plans of intravaginal therapy. *Radiology*, Oct., 1947, *48*, 462–475.

The practical limitations of intravaginal therapy are discussed at some length. Twelve theoretical methods of intravaginal roentgen therapy are presented, and the distribution of radiation calculated from published depth dose data. To compare the plans, the number of roentgens reaching the midline at the level of the internal and external os, and at points 2 and 4 cm. lateral to the midline and 2 cm. in an anteroposterior direction from the midline were calculated. The variations in the method of treatment for one, two and three field techniques were: changes in quality (half-value layer); alterations in size of a beam; changes in direction of the beam of radiation; dose applied per field, as well as total vaginal dose.

The first four plans utilize one field centered on the cervix. Because of the danger of necrosis in one field treatment plans with circular transparent cones, doses are limited to a dosage level of 8,000 to 10,000 r in air, and the area of effective irradiation extends for about 3 cm. from the midline at the level of the internal os.

The next four plans are presented to show the effects when high voltage radiations are sacrificed to achieve greater angulation of the beam by lateral direction of the cone. Different qualities of radiation are compared, the total dose delivered kept at 6,000 r or 12,000 r per field; 12,000 r is too much for softer types of radiation, as fairly wide areas of probable necrosis are indicated. However, radiations of 0.5 mm.

Cu half-value layer (140 kv., 25 mm. Cu filter) yield no area of necrosis.

Plans 9 to 12 utilize one straight cone and two angulated cones, the quality, dose and angulation kept constant, but the size and position of the cones varies. Three cones 3 cm. in diameter, with the lateral one angulated at the mid-point of the cervix, resulted in too much overlapping. A large central cone (4 cm. in diameter) with lateral one 2 cm. in diameter, placed in the fornices and angulated at the lateral edge of the cervix, did not yield very effective radiation at the level of the internal os. With a large central cone 4 cm. in diameter and two lateral cones 3 cm. in diameter, a more effective spread of radiation could be achieved with 6,000 r delivered by the lateral cones.

The authors conclude that: (1) the one field treatment plan is limited by the reaction to irradiation at the level of the external os, and does not control cancer in the lateral parametria. They believe it could well be used at a lower dosage as a preliminary to radium implantation, and in cases of carcinoma of the cervical stump where radium implantation is diffcult; (2) the two field method is inadequate for control of tumor cells confined to the cervix itself. The combination of intracervical tandem and interstitial needles might well complement the two field method; (3) the radiation distribution for the three field method of treatment would seem as effective as that obtained from intracavitary or interstitial radium. Intravaginal roentgen treatment carried to its maximum could be used without radium. (4) The authors expect from such procedures an improvement in clinical results.—*Gordon J. Culver, M.D.*

Neary, G. J. Physical aspects of intracavitary radium treatment of carcinoma of the cervix uteri. Part III. A New Applicator. *Brit. J. Radiol.*, Nov., 1947, *20*, 454–469.

In a previously published analytical treatment of the problem, the factors influencing the dose distribution in intracavitary radium treatment of carcinoma of the cervix uteri were investigated. It was concluded: that little fundamental improvement in the distribution of the radiation dose by modification of the basic Paris or Stockholm techniques is to be expected; that radium in the vagina should be concentrated in the midline; that the only way to increase the dose near the lateral pelvic wall is to increase greatly the quantity of radium in the vagina; and that this necessitates the use of heavy metal absorbing screens for protection of the rectum as well as other midline structures.

An ingenious applicator has been designed which uses 70 milligrams of radium in the uterus and two units of 140 mg. each in the vagina. The treatment time is seventy-two hours. The distribution of the radiation depends upon an arrangement of massive platinum filters. An important factor is the separation of the two portions of the vaginal radium by a heavy wall of platinum. This markedly reduces the dose to the vaginal mucosa and does not materially reduce the dose to the parametria. The entire lower half of the applicator is a heavy platinum filter for the rectum. Other specially shaped screens are incorporated into the applicator to control the dosage to the various portions of the pelvis. The uterine portion of the applicator is firmly fixed to the vaginal part and the latter is large enough to fill the upper vagina. The applicator weighs about $2\frac{1}{4}$ pounds. It is held in place by its firm fixation to a harness which is fixed in relation to the bony pelvis. Thus the entire applicator does not change position with change in position of the patient.

Complete isodose curves are presented for this applicator. The total energy absorption for a treatment is about 13.0 megagram roentgens as compared with 9.2 megagram roentgens for a typical Stockholm treatment.

Improvements which are to be anticipated are the use of uranium as a screening material to replace platinum and greatly reduce the cost of the applicator, and the use of certain radioactive isotopes instead of radium which will permit the use of millimeters of lead instead of centimeters of platinum in the screening materials.—*E. F. Lang, M.D.*

Speert, Harold. Late recurrence of cervical carcinoma following radiation therapy. *Am. J. Obst. & Gynec.*, March, 1948, *55*, 533–537.

Recurrence of carcinoma of the cervix after irradiation almost always occurs within less than five years. The author reports 2 cases in which the recurrence took place seventeen and one-half years and nineteen and one-half years after previous irradiation to carcinoma of the cervix.

In the first case the anatomic diagnosis in a fifty-two year old woman at death was "carcinoma primary in the cervix with extension to

the fundus, bladder, rectum, ovaries, Fallopian tubes, and metastatic invasion of periaortic lymphnodes, liver, and diaphragm; ureteral obstruction, bilateral, with hydroureter and hydronephrosis." More than three-fourths of the uterus was involved by the tumor mass. Microscopic sections at death were compared with slides made seventeen and one-half years before and the two sections were completely similar in histopathologic detail. The anaplastic nature and somewhat unusual histopathologic appearance of the cells of this tumor strengthens the impression that this was a recurrent tumor and not a new carcinoma of the cervix.

The second patient died at the age of fifty-four years with the tumor involving the bladder and rectum and with a vesicovaginal fistula and a rectovaginal fistula. Nineteen and one-half years prior to this time she had been treated with radium and roentgen rays for carcinoma of the cervix following which she was free of symptoms until several years prior to death when she experienced a foul blood-tinged vaginal discharge which persisted until death. The microscopic sections from the original cervical tumor and from the tumor at death showed epidermoid carcinoma in each case. The author feels that it is more difficult in this case than in the first to definitely prove that this is a recurrent tumor rather than two separate tumors, although she was followed in the same clinic carefully for several years after the cervical tumor was originally treated and again for the last few months prior to death so that he is reasonably certain that this was a recurrent tumor.—*Wendell C. Hall, M.D.*

BOWING, HARRY H., and FRICKE, ROBERT E. Late results of radium therapy for carcinoma of the uterine cervix. *J.A.M.A.*, July 10, 1948, *137*, 935–942.

Results of all cases (2,246) treated at the Mayo Clinic for carcinoma of the cervix by radium therapy between 1915–1944 inclusive are analyzed.

Surgery has always been maintained at the Clinic; as a result, irradiation has proved to be an excellent surgical "adjunct," otherwise radium is chosen for treatment of patients in the operable, further advanced and recurring groups. Close to 60 per cent of all cases of cervical carcinoma, including those operated upon, received some combination of radium and roentgen therapy. The number of early or favorable cases in which treatment for cure may be possible is practically always low, an estimated 10 to 15 per cent of the total. This compares with a figure of 11 per cent selected for surgical intervention. Among the favorable cases referred for radium, more are found with obesity, and other constitutional diseases as well as older patients, than are to be found among those chosen for surgery.

According to age grouping the largest number reported in the fourth decade with the numbers dropping off rapidly, both younger and older. On analysis of the age groups the authors contend that the patient of forty-nine years or less has a mildly unfavorable factor influencing her five year cure rate while the patient over forty-nine years of age carries this additional favorable factor.

They have aptly summarized the League of Nations classification as to extent of the disease as follows:

Stage I	Lesions confined to the cervix.
Stage II	There is a moderate local invasion.
Stage III	There is extensive local invasion or unilateral fixation.
Stage IV	There is a massive local invasion or metastasis elsewhere.

Only 1.3 per cent of the total number are classified as Stage I, while the majority, 66 per cent, are listed as Stage III. Comparing the stage of the disease as against the mean age in years gave the interesting fact that the mean age averages slightly above or below fifty for all stages. The youngest mean age group (46.4 years) represented those who had undergone some operative procedure such as cauterization or amputation of the cervix before reporting for admission to the Clinic. In attempting to analyze the five year survival rate as compared to the age grouping, much of the authenticity is lost due to the proportionately small percentage of patients traced (varying from 25 per cent to 43.6 per cent). This difficulty is of course explained by the fact that patients after discharge scatter widely to their homes.

Study of the grade of malignancy (Broders' grouping) brings out the fact that the highest percentage of survival of "traced" patients, 57.1 per cent, are grouped as Grade I and the lowest, 19 per cent, represent that group which the pathologist has failed to grade for various reasons. The authors admit that radiosensitivity is more complex than the microscopic analysis of the tissue; other factors which have an

important bearing on prognosis include the blood supply to the tumor bed, as well as the judgment, skill and radium technique applied by the radiosurgeon.

The authors individualize their technique with the interval between radium application prolonged where the response to treatment is prompt and shortened where the response is prolonged. Patients with serious local complications as inflammation, ulceration, necrosis and bleeding are seen and treated almost daily. Total radium treatment time for the average Stage III patient is about three weeks. Roentgen therapy is begun on the final day of radium treatment. Two anterior and two posterior pelvic ports are outlined giving a total of 500 to 700 r per field. This roentgen irradiation cycle may be repeated after a three month interval. Follow-up consists of re-examination every three to four months for the first post-treatment year, every six months for the second post-treatment year and yearly thereafter.

The five year survival rate is modified in that those patients lost to follow-up are not included in the final figure. Interestingly enough a higher per cent of Stage II traced cases (65.3 per cent) survived five years than Stage I traced cases; this is partly accounted for by the fact that only a small number in Stage I (10) were traced for five years. Five year cures, however, occurred in all classifications. There were five deaths, a hospital mortality of 0.2 per cent. The serious morbidity rate was equally low.—*William E. Howes, M.D.*

RADIOISOTOPES

Henshaw, P. S., Riley, E. F., and Stapleton, G. E. The biologic effects of pile radiations. *Radiology*, Sept., 1947, *49*, 349–360.

Experiments were carried out with strains of mice to determine the late effects of periodic and single exposures of penetrating radiations (fast neutrons, slow neutrons, gamma rays, and beta rays). In general, the late effects of penetrating radiations consisted of generalized atrophy and neoplasia of hemopoietic organs. Neoplasia may or may not result directly from the atrophic condition.

Different thresholds of damage were found. Survival time, one of the most sensitive responses, showed effects following daily exposures in the range of 0.1 n of fast neutrons and 1 r of gamma rays. Threshold responses of the peripheral blood were often less sensitive than the threshold survival responses. Threshold levels were not determined for single exposures.

The r/n ratio of gamma rays to fast neutrons for the different effects varied roughly from 8 to 1 to 35 to 1 for the conditions and methods used.

The accumulated evidence indicates that the degree of biologic effect varies not only with the dose but also with the density of ionization produced.

The incidence of lymphoma following exposure to penetrating radiations was raised from 15 per cent in the controls to over 60 per cent in groups receiving single doses of 500 and 700 r of gamma rays.

Lung tumor incidence was increased little, if any, by the treatments given. Many types of skin carcinomas developed following sublethal doses of beta rays. It is significant that hemopoietic tissue tumors were obtained with penetrating radiation and skin tumors with surface-absorbed radiations.—*Paul R. Dirkse, M.D.*

Dougherty, E. C., and Lawrence, J. H. Isotopes in clinical and experimental medicine. *California Med.*, July, 1948, *69*, 58–73.

All of the known 96 elements exist in several nuclear forms. Of the 81 stable elements, 60 have more than one stable isotope. Over 600 unstable isotopes are known, including at least one for each of the 96 elements. Only 7 stable isotopes have found biological use, but over 70 unstable isotopes have had some biological application.

Clinical use of radium and its decay products is well known, and constitutes one type of isotope application. Artificial isotopes of phosphorus and iodine have an established therapeutic value. Others have received preliminary trial. Usefulness depends on, and is limited by, the degree of selective localization in tissues or organ systems. For example, radiophosphorus concentrates in the nucleoprotein fraction of rapidly growing tissue, radioiodine localizes selectively in the thyroid gland, and certain isotopic colloids may be largely localized in selected parts of the reticulo-endothelial system. Ideally, successful use of radioisotopes in therapy of neoplasms might include radiohydrogen or radiocarbon; the beta rays of these isotopes have a penetration range of the same order as the diameter of a neoplastic cell.

Radiophosphorus in Therapy and Diagnosis. In polycythemia vera, several years of complete

hematological and symptomatic remission may be obtained with radiophosphorus therapy. Retreatment is usually necessary within three years. In chronic leukemia, radiophosphorus appears to be as satisfactory as roentgen therapy, and it may prolong life somewhat further. It has the advantage of not producing radiation sickness, but may result in anemia, thrombocytopenia, or leukopenia. In a series of over 300 patients with chronic leukemia treated with radiophosphorus, average duration of life after onset of symptoms was almost five years, and over 30 per cent have lived over five years.

Miscellaneous applications of radiophosphorus include local application to skin lesions, and interstitial injection into tumor areas. Exploration of its diagnostic possibilities has begun with the demonstration of counter-detectable localized radioactivity in superficially located rapidly growing tumors.

Radioiodine in Therapy and Diagnosis. Oral administration of radioiodine is a simple and effective method of controlling or curing many cases of hyperthyroidism. Occasional adenocarcinomas of the thyroid with iodine-metabolizing metastases respond favorably to radioactive iodine. Radioiodine is useful in demonstrating levels of thyroid hypofunction or hyperfunction, and may be used to distinguish between simple hyperthyroidism and the ophthalmopathic type.

Other Radioisotopes in Therapy and Diagnosis. Radiosodium has been used in chronic leukemia, but lacks the selective localization of radiophosphorus. Its effects are comparable to that of total body irradiation. Radiosodium has been found useful in estimating circulatory adequacy of the extremities in certain vascular diseases.

Radiostrontium has had trials in the therapy of malignancy in bone, as its distribution in the body follows that of calcium. Radioactive colloids have shown selective localization in the reticuloendothelial system which may prove useful. Anhydrous chronic phosphate, which may be tagged with radiophosphorus, localizes almost entirely in the liver and spleen. Radioisotopes of yttrium, zirconium, columbium, and gold may, depending upon the method of preparation, concentrate in the liver and spleen, or go in equal concentration into the bone marrow. Colloidal manganese dioxide, and possibly radioactive gold as well, may be localized selectively in the lymphoid tissue. Interstitial infiltration of neoplasms with zinc or gold radioactive colloids has resulted in effective localization and in tumor regression.

Certain isotopes, such as those of lithium, boron, and fissionable isotopes such as uranium and plutonium, release large amounts of ionizing radiation upon being bombarded with slow neutrons. If such material can be localized in given tissues or tumors, and the region subjected to slow neutron bombardment, a higher radiation can be conferred on the isotope-containing tissue than on the uninvolved tissue through which the neutrons must pass. A few experimental studies of this principle, using mouse tumors, have shown the predicted enhanced effect.—*Henry P. Brean, M.D.*

KNAUSS, HAROLD P. Slide rule calculations of radioactive decay. *Science*, March 26, 1948, *107*, 324.

This article describes the use of the ordinary slide rule in making calculations on the decay of radioactive substances. Details of the use of the slide rule for this purpose are given.

LISCO, HERMANN, FINKEL, MIRIAM P., and BRUES, AUSTIN M. Carcinogenic properties of radioactive fission products and of plutonium. *Radiology*, Sept., 1947, *49*, 361–363.

An intelligent appreciation and evaluation of health hazards, whether by ingestion or inhalation or by wound contamination with small amounts of radioactive substances, is difficult without experimentation. These experiments were undertaken with this in mind, even though it was realized that it is notoriously difficult to design animal experiments which precisely duplicate the human hazards.

Radiostrontium (Sr^{89}) is largely concentrated in bone, and consequently bone tumors were readily produced. The incidence was approximately proportional to the dose, and the latent period—not less than about 200 days—increased with decreasing dose. Bone tumors were produced by doses ranging from 5.0 to 0.05 microcurie per gram, both with single and with monthly repeated injections. Radioactive yttrium (Y^{91}) and cerium (Ce^{144}) also produced sarcomas in the skeletal system, primarily in the long bones. Plutonium (Pu^{239}) and yttrium (YPO_4) produced local radiation damage when given subcutaneously and intramuscularly in mice. Many local fibrosarcomas were also produced at doses of 0.5 to 0.05 microgram per gram of Pu^{239} and doses of 1.5 to 0.05 micro-

curies per gram of YPO_4. Bone tumors resulted frequently in different animals injected with Pu^{239} at levels of 4.5 to 0.05 micrograms per gram, again with a latent period of about 200 days. These tumors occurred mostly in the spine, since plutonium has a greater affinity for collagenous tissue than for bone proper, while those from strontium were chiefly in the long bones.

Both plutonium and cerium showed a high concentration in the liver and frequently produced liver damage, but no true liver tumors have been seen to date. Y^{91}, which when fed by stomach tube remained longest in the colon, produced several carcinomas of the colon in rats, in the higher doses used.—*Paul R. Dirkse, M.D.*

Stanley, Malcolm M., and Astwood, E. B. The accumulation of radioactive iodide by the thyroid gland in normal and thyrotoxic subjects and the effect of thiocyanate on its discharge. *Endocrinology*, Feb., 1948, *42*, 107–123.

As others have found, thyrotoxic patients had a larger uptake of radioactive iodine in the thyroid than normal patients. After the administration of thiocyanate or ordinary iodide, the radioiodine also was more rapidly discharged. These differences, the authors feel, are great enough to provide an accurate means of detecting thyrotoxicosis.—*John W. Karr, M.D.*

MISCELLANEOUS

Best, Arthur, and Stroud, Leona. A method of x-ray reproduction of the negative x-ray film. *Am. Rev. Tuberc.*, Feb., 1947, *55*, 184–186.

The negative 14 by 17 inch roentgen film to be reproduced is placed in the cassette next to the top as opening screen of the cassette. An unexposed film is then placed next to the negative roentgen film and between it and the back screen of the cassette is placed the black protecting paper that always accompanies an unexposed film. The purposes of the black protecting paper is to prevent any fluorescence emanating from the back screen of the cassette.

The following technique is then employed: 40 inch distance, 100 milliamperes, 42 kilovolts (peak) and one-half record. The roentgen film is then developed in the usual manner. By the same technique, a negative reproduction of the positive reproduction can further be made if this is desired.—*J. J. McCort, M.D.*

Camp, John D. A grid-front cassette; a useful application of the stationary grid. *Radiology*, November, 1947, *49*, 627–628.

A method by which any make cassette can be converted to a grid-front cassette is described. The ordinary bakelite front is replaced by a metal Lysholm grid of proper size, and protected by a plastic covering. The original thickness and size of the cassette are maintained.

Use of a grid-front cassette has improved the detail of portable roentgenograms and facilitated rapid sequence exposures, where Potter-Bucky technique is slow. Extreme usefulness compensates for the rather high cost.—*George P. Keefer, M.D.*

Goldfeder, Anna. Further studies on the relation between radiation effects, cell viability, and induced resistance to malignant growth. *Radiology*, December, 1947, *49*, 724–732.

This article is number four in a series and is a comparison of effects of roentgen rays on mammary tumors autogenous to inbred strains of mice (dba and C3H.) The tumors of both strains were diagnosed as adenocarcinoma, but they varied in clinical characteristics. The percentage of tumor "takes," the latent period (time between transplanting and the development of a measurable tumor), and the size of the tumor formation were distinctly different in the strains.

The experiments described in the article clearly show that the radiosensitivity of tumors of similar histopathological structure is variable and that the recovery process or "latent period" of similar tumor cells partially affected by irradiation is also variable. The author concludes that histopathologic classification alone is not a conclusive guide to the specification of a proper therapeutic dose for any given tumor.—*Richard E. Kinzer, M.D.*

Clark, George L. Medical, biological and industrial applications of monochromatic radiography and microradiography. *Radiology*, October, 1947, *49*, 483–495.

Roentgen-ray diffraction analysts have long made use of tubes which produce essentially monochromatic beams in contrast to the usual

polychromatic beam used in the various branches of roentgenography.

Above a certain critical voltage, different for each target element, the spectrum characteristic of the element appears superimposed on the continuous spectrum, with the result that certain wavelengths are greatly intensified. To isolate one of these characteristic intensified beams would be to produce a monochromatic beam. To accomplish this strictly requires selection and reflection by a crystal, but the very great loss of energy renders the method impractical. Less exact, but practical and in common use, is employment of a characteristic filter which cuts out all shorter wavelengths.

Production of a monochromatic beam from a tungsten target tube is impractical because the characteristic tungsten spectrum does not appear until a voltage of 69,300 has been surpassed (where the general radiation intensity is high), and because a very rare element, either lutecium or ytterbium, is required for the filter. But a molybdenum target tube will generate an intense characteristic spectrum at 20,000 volts where the general radiation is still weak and a very thin layer of a zirconium compound will serve as an effective filter. Copper, cobalt, and chromium target tubes are also practical.

The performances of a polychromatic beam produced by a tungsten target tube and a monochromatic beam produced by a molybdenum, copper, cobalt, and chromium target tubes were compared when identical voltage, focal spot sizes, focal spot-target distances, target-film distances, film, and simultaneous development were employed.

Appreciably greater definition in fine detail is produced in monochromatic roentgenograms. Examples from industry (hair-line cracks in aluminum castings), biology (pine seeds, frogs), and medicine (bones of the hand) are illustrated. Detection and demonstration of early disease may be aided by monochromatic roentgenography.

Monochromatic roentgenography is a research tool of unlimited, but as yet almost untested, potentiality, for it can be used to supplement and augment the microscope. In microroentgenography, images are registered on extremely fine-grained photographic emulsion by a monochromatic roentgen-ray beam. The technique is described and is quite simple. The images may then be enlarged up to 400 diameters. Several biological specimens are illustrated. The results obtained are striking and stimulating.—*George Cooper, Jr., M.D.*

PROSSER, C. LADD. The clinical sequence of physiological effects of ionizing radiation in animals. *Radiology*, September, 1947, *49*, 299–313.

In order that the clinical effects of irradiation be understood and methods of therapy be explored and made available, research problems in clinical physiology and biochemistry were carried out at the Metallurgical Laboratory of the University of Chicago under the Manhattan Project. The problems have been concerned with (1) ascertaining whether different kinds of ionizing radiation have similar effects upon the mammalian body; (2) measuring sensitive reactions as a function of dose, in the hope of setting permissible exposure limits; (3) searching for sensitive biological indications of exposure; (4) describing the course of radiation damage sufficiently to suggest profitable directions for research into mechanisms of such damage that might eventually lead to effective therapy. None of these objectives has been attained in a final form, but sufficient data are available to justify a summary at this time. The pattern of clinical effects of irradiation fall into the following periods: (1) initial, (2) acute, (3) subacute, (4) chronic. The effects of whole body irradiation were observed on different species of animals. Alterations were observed during the various periods in the gastrointestinal, circulatory, hemopoietic, liver, respiratory, and nervous systems.

Four generalizations can be presented on the basis of the observations made:

I. Every kind of ionizing radiation is similar in its clinical action, whether it be penetrating external radiation or internal radiation from deposited material. A similar clinical course can be observed by single and daily roentgen irradiation, and with internal radiation from deposited alpha and beta emitters (by selecting the appropriate dose, dose rate, and experimental animals). Although not studied in as great detail it appears that the clinical pattern is similar after treatment with gamma rays, fast neutrons, and slow neutrons.

II. Nearly every organ system is affected by lethal doses of every type of radiation. The most sensitive systems are the blood forming organs, the gastrointestinal tract, and the go-

nads. Peripheral circulation and heart are also affected. Terminally there may be damage to the kidneys and even to the central nervous system.

III. No single clinical reaction is peculiarly specific for irradiation damage. A similar preterminal course can be observed with toxic agents such as the nitrogen mustards; acute infections; anaphylactic shock; and various toxic chemicals, e.g., anemia in benzol and phenyl hydrazine poisoning.

IV. The clinical picture and the conditions resulting in death vary with the dose rate and the duration of exposure for both external and internal radiation. If an animal survives one depression with a given set of symptoms, it is likely to die later from a different mechanism.

A series of clinical patterns leading to death after irradiation have been identified as follows:

1. Immediate death at very high doses and dose rates with general cellular destruction.

2. Initial shock-like death seen within forty-eight hours after roentgen irradiation in some rabbits and chickens.

3. Early deaths at high doses in dogs and rats (four to six days). There is evidence of dehydration, hemoconcentration, and much gastrointestinal damage and leukopenia.

4. Acute deaths caused by irradiation from all types of ionizing radiations (except external beta rays) occur nine to twenty-one days after treatment. Severe leukopenia, extensive tissue breakdown, tendency to bleeding, high sedimentation rate, slight anemia, and altered water balance are observed. The terminal condition is one of toxemia with fever, elevated heart rate, lowered albumin and elevated globulins, high serum nonprotein nitrogen, increased serum protein, cardiovascular failure, and so forth.—*Robert K. Arbuckle, M.D.*

Barclay, A. E. Microarteriography. *Brit. J. Radiol.*, Oct., 1947, *20*, 394–404.

During an investigation of traumatic uremia in rabbits, results suggested the existence of a vascular short cut between the arteries and veins which could leave the cortex ischemic. Ordinary roentgenographic techniques failed to show any communication, and a new method was sought to demonstrate the minute vascular structures. After some preliminary experimentation, a hot cathode diffraction tube with a beryllium window was used which gave a constant beam between 5 and 50 kv. at up to 20 ma.

The rabbit kidney is injected either in vivo or after removal. Several media may be used. Thorotrast gives excellent results. Ten per cent colloidal gold or specially prepared colloidal bismuth are not only radiopaque but can also be seen in microscopic study. After injection, the kidney is fixed in the usual manner and the entire organ roentgenographed. After determination of the direction for sectioning which will give the maximum vascular pattern, sections are cut. The sections between 120 and 450 micra were most satisfactory.

Roentgenograms are made on Kodak Maximum Resolution plates. Since the sensitivity of this is much reduced when it is wet and since the sections must be kept moist with glycerine to prevent shrinkage and distortion, a thin tissue is used as a barrier between the section and the film. The most satisfactory is found to be the tissue used for the heat mounting of prints. As the sections are exposed to the air, the exposure is made as short as possible. At a distance of 8 inches, at 20 ma., and at 15 to 20 kv. a 240 micron section requires an exposure of about five minutes. If the section is thin and softer rays must be used, a shorter distance is necessary with greater distortion. The cassettes are built to fit over the end of each cone in a light-tight manner, so that the tube, section, and film are one unit. The cassette must be applied to the cone in the darkroom as there is no cover between the section and the roentgen tube, so that the maximum use is made of soft roentgen rays.

The resulting negative may be enlarged with standard apparatus and the whole section studied, but above a magnification of 10, detail is a limiting factor. On the other hand, if a small field is used a photomicrograph may be made and this in turn enlarged. This process, surprisingly, preserves the detail much better, and satisfactory magnification of 250 diameters can be obtained. This method has the disadvantage of utilizing only a very small segment of the negative.

Using this method, stereoscopic views of the entire organ were made to determine the course of the vessels, and sections were made. These were again examined stereoscopically and further sections in appropriate planes were made to show the finest vascular structures in a section 240 micra thick. Thus the picture of

the vascular supply of the organ can be built up as a whole.—*E. F. Lang, M.D.*

LOVERDO, ANDRÉ. Sur l'emploi de gants de protection radiologique chargés à l'oxyde de thorium (ThO_2). (On the use for radiological protection of gloves laden with thorium oxide.) *Compt. rend. Soc. de biol.*, June, 1948, *142*, 843–844.

Rubber gloves into which thorium oxide has been incorporated—average thickness of 0.5 gm/sq. cm.—has been tested for radioactivity with a G-M scaler. The following ionizing energies (as absorbed per gram of tissue in contact with the glove) have been computed: (a) 0.011 r.e.p. per hour due to the beta and gamma radiations, (b) 1.38 r.e.p. per hour due to alpha radiation. These figures have already been corrected for self-absorption and angular distribution and represent the average as to the depth effect. The quantity of beta and gamma radiations would fall within the limits of the American norm of radiological safety dose (supposing that the gloves are worn intermittently) but that of alpha radiation is definitely beyond the safety limit, especially for the superficial 0.1 mm. of the epidermis (which includes the layer of Malpighi). The author advises the use of a supplementary rubber glove to absorb the alpha radiation. He asks for such a modification in the fabrication of the gloves.—*J. N. Sarian, M.D.*

BARRON, E. S. GUZMAN; BARTLETT, GRANT R., and MILLER, ZELMA B. The effect of nitrogen mustards on enzymes and tissue metabolism. I and II. *J. Exper. Med.*, June, 1948, *87*, 489–520.

I. *The Effect on Enzymes.* The halogenated alkylamines ("nitrogen mustards") have certain biological properties similar to those of the roentgen ray: injury to bone marrow and lymphoid tissues, inhibition of mitosis, and production of mutants which have been the basis for their use in treatment of blood dyscrasias. When placed in neutral aqueous solution, these substances form ethylenimonium-ring compounds which are structurally similar to choline and acetylcholine, and evidence is presented indicating that they function as structural inhibitors of these enzymes, uniting with their protein portions at the side chains where combination with choline and acetylcholine usually occurs. Tiosulfate breaks down the ethylenimonium derivatives, and its presence prevents this inhibiting activity.

Nitrogen mustards also react rapidly with —SH (sulfhydryl) groups of many intermediate products of both protein and carbohydrate metabolism, some of which are essential to enzyme activity, and thus one might expect a large number of enzyme systems to be inhibited by them, but in vitro experiments do not bear this out, showing only the choline ozidase, acetylcholine esterase, and pyruvate ozidase systems to be inhibited in concentration under 10^{-3}M ($10 \times LD_{50}$). This structural inhibition is quite specific and is irreversible.

A list of the enzyme systems inhibited by these substances is given.

II. *The Effect on Tissue Metabolism.* As studied in metabolism of tissue slices and of leukocytes, and in tissues of treated animals, tissue respiration is strongly inhibited and tissue glycolysis is very little affected by nitrogen mustards. Pyruvate metabolism is profoundly inhibited. Certain oxidative and biological synthesis processes are listed as showing distinct inhibition which can readily promote cell destruction and depress the formation of new cells.

Choline was found to protect marrow cells from the respiratory inhibiting effect of nitrogen mustards, and possible development of a method to avoid toxic marrow effects by use of such a substance in treatment is suggested.

The authors propose the explanation of mitosis inhibition by nitrogen mustards, sulfur mustards, and roentgen rays on the basis of a process controlled by a sulfhydryl enzyme with very labile and reactive —SH groups, alkylated by the mustard compounds and oxidized as a result of irradiation.—*Joseph B. Stull, M.D.*

FREED, JOHN H., FARRIS, EDMUND J., MURPHY, DOUGLAS P., and PENDERGRASS, EUGENE P. Effect of low dosage roentgen radiation on the gonadotropic function of the hypophysis of the mature and immature female albino rat. *J. Clin. Endocrinol.*, June, 1948, *8*, 461–481.

A review of the literature on treatment and results of low voltage roentgen therapy in the treatment of functional menstrual disorders and sterility convinced the authors that its mode of action is still poorly understood. They note that many theories have been proposed to

explain the good results reported clinically in hypofunctional endocrine conditions and that these may be divided into two groups: (1) stimulation; (2) selective destructive action. From a survey of the experimental literature they conclude that low voltage radiation of the pituitary, with doses of 400 r (air) or less, has shown no histological effects on the sexual systems of animals. Furthermore, that the immediate and latent effects were seldom carefully observed. In view of the importance of this highly controversial problem they felt that further investigation was necessary using methods designed chiefly to evaluate the physiological effects.

From their experiments the authors draw the following conclusions:

1. Low dosage radiation of the pituitary can produce a transient effect on the normal pituitary function of the rat. Though the immediate physiological effect is in the nature of a stimulus such an effect is only transient and not prolonged.

2. Irradiation of the pituitary in small doses has no effect on the normal development of the sexual system of immature twenty-eight day old female rats.

3. There is no evidence that roentgen irradiation can stimulate living cells, if by stimulation is meant a continued acceleration of their normal growth or function.

4. Irradiation of the pituitary in small doses has no evident harmful effect in the experimental rat.—*Charles G. Stetson, M.D.*

Holmes, Barbara E. The inhibition of ribo- and thymo-nucleic acid synthesis in tumor tissue by irradiation with x-rays. *Brit. J. Radiol.*, Nov., 1947, *20*, 450–453.

In similar rat sarcomas from the same source, the content of ribo- and thymo-nucelic acid is surprisingly constant. A number of rats with a given rat sarcoma was treated after injection of radioactive phosphorus (P^{32}), and the amount of the nucleic acids determined by the amount of this substance present. It was found that the formation of thymo-nucleic acid was markedly decreased by irradiation when compared with the control group of tumors. The same effect was produced in ribo-nucleic acid but to a less marked degree. Nembutal also was found to inhibit the activity in formation of both ribo- and thymo-nucleic acids.—*E. F. Lang, M.D.*

Allen, J. Garrott; Sanderson, Margaret; Milham, Mary; Kirschon, Alice, and Jacobson, L. O. An anticoagulant in the blood of dogs with hemorrhagic tendency after total body exposure to roentgen rays. *J. Exper. Med.*, Jan., 1948, *87*, 71–86.

In times past the hemorrhagic state which along with infection is one of the most important pathological changes following large doses of radiation, has been attributed to the associated thrombocytopenia, but from the experimental evidence described in this report a substance similar to heparin is indicated. It can be biologically inactivated by intravenous protamine sulfate or by toludine blue which restore the clotting time to normal although it had been prolonged to four days in spite of normal platelets, fibrinogen, prothrombin and calcium and the administration of vitamin K.

The presence of this anticoagulant (heparin-like) substance may be demonstrated several days before other evidence of disease and before the development of the eventual thrombocytopenia. It also causes a gel formation that is quite easily broken down by shaking (this same phenomenon occurs in heparinized blood).

Attempts to isolate heparin were unsuccessful but this is not surprising in view of the very inefficient methods available which yield only a 5 to 15 per cent recovery of a known heparin sodium acid salt.

In this experiment 25 dogs were irradiated with 200 kv. roentgen rays, receiving in one dose to entire body, 450 r (0.5 mm. Cu plus 1 mm. Al filtration; 15 ma., dosage rate 6 r/min. in air at a distance corresponding to the center of the animal's body).—*Joseph B. Stull, M.D.*

Bloom, William. Histological changes following radiation exposures. *Radiology*, Sept., 1947, *49*, 344–348.

A large series of animals were exposed to a variety of internal and external sources of radiation, including roentgen rays, fast and slow neutrons, gamma rays, beta rays, and internally administered radium, plutonium, sodium,^{24} phosphorus,^{32} barium,^{140} lathanum,^{140} strontium,^{89} zirconium, yttrium,^{91} and radiocerium.

Animals were given LD50/30-days dose and fractions thereof in the hope of finding the lower limit of irradiation damage as shown by the microscope.

Irrespective of the particular external sources, the author was unable to tell which type of radiation had been used on the animals, except for external beta rays since the changes were practically limited to the skin with that source. After the injection of radioactive material, the damage qualitatively was the same with all of the materials, and the same results were produced as by the external irradiations, modified only by (a) whether the materials reached a particular organ and (b) the type of particle emitted by the radioactive isotope. The differences are due to focalization.

In general, no histopathologic evidence was found for the cause of death. That is, no differences could be seen between the animals which died with an LD50/30-days dose and those which did not die after the same dose. The author was impressed by waves of destruction in some of the animals that received high doses, so that one could speculate on somatic mutations but there was no evidence on this point.

In general a particular organ showed histopathologic changes reflecting the amount of radiation rather than species, although one animal will tolerate much higher doses than another.

With both total body external irradiation and with internal sources of radiation no evidence whatever of any primary stimulating effect of small doses was obtained. Either a damaging effect was found or no difference from the control animals.

Striking exceptions were also found to the theory that the more primitive the cell, the more susceptible it is to radiation. A more interesting part of the problem has been the general question of why certain strains of cells are sensitive and others very resistant. After more than three years' association with this project, the author has not even a clue on which to speculate. No relation to mitotic activity was found.

Evidence was found on the question of the sensitivity of the erythroblasts. In the material used, these were exceedingly sensitive to radiation, about as sensitive as the lymphocytes.—*Paul R. Dirkes, M.D.*

Fredericq, J., and Chèvremont, M. Etude histologique et histochimique de la peau de cobaye traitée par les rayons X. (Histological and histochemical study of the skin of guinea pig treated with roentgen rays.) *Comp. rend. Soc. de biol.*, June, 1948, *142*, 850–853.

After a short historical introduction, the authors state that they were interested in the sulphydril group histochemical changes in the irradiated epidermis as this group is of importance in the keratinization processes. The skin of the hind paws of some 11 guinea pigs were irradiated with single doses of 3,000 r per paw (10 were irradiated with either 1,500 r or 2,000 r, the results obtained being almost the same in all 21.) The factors of irradiation are not given (except for 1 mm. Al filtration and target skin distance of 33 cm.)

After a very marked thinning and destruction, the epidermis begins to regenerate from the borders of the lesion and soon attains a thickness exceeding greatly that of the non-irradiated skin. However it is of an abnormal appearance. The histochemical studies reveal a considerable decrease in the —SH (—Sulphydril) groups at the irradiated regions. Later on, as the regeneration starts, there is a great increase. This initial decrease does not seem to be due to a direct action of the roentgen rays on the —SH groups. In the non-irradiated parts of the skin of these experimental animals, there is elicited a temporary diminution of —SH groups.—*J. N. Sarian, M.D.*

SUBJECT INDEX TO VOLUME 61

(abs) = abstract (E) = editorial

Abscess, unilateral paraspinal (abs), 436
Acoustic nerve, tumors of (abs), 264
Acridine compounds, in vivo staining and retardation of tumors in mice by (abs), 287
Acromegaly presenting specific roentgenographic changes (abs), 281
Adenocarcinoma of jejunum, 680
of stomach, and co-existent benign gastric ulcer, 677
Adenoma, bronchial, without signs of bronchial obstruction, 209
Adrenal tumor of liver in child (abs), 432
Afferent fibers, visceral, investigation of (abs), 130
Alimentary function, roentgen signs of altered, following autonomic blockade with tetraethylammonium (abs), 733
Amebiasis with pulmonary involvement (abs), 122
American Board of Radiology, certification of radiation physicists, 116
inspection of training facilities in radiology by, 728
American College of Physicians, research fellowships, 862
American Radium Society, preliminary program of Thirty-first Annual Meeting, 568
Anatomy of lesser circulation, indicated by its behavior in health and disease, 1
roentgen, of oblique views of lumbar spine, 699
Aneurysm, aortic, secondary to coarctation (abs), 275
Angiocardiography, value of, in establishing diagnosis of pericarditis with effusion, 41
Angiography, cerebral, differential diagnosis of intracranial neoplasms by (abs), 265
cerebral, technical improvements in (abs), 426
direct cerebral, technique of (abs), 266
intracranial, practical serialograph for, 324
vertebral, 166
Ankle, osteochondritis dissecans of (abs), 435
Anticoagulant in blood of dogs with hemorrhagic tendency after total body exposure to roentgen rays (abs), 885
Aorta, aneurysm, secondary to coarctation (abs), 275
coarctation of, surgical treatment for (abs), 123
occurrence and diagnosis of dilatation of, distal to area of coarctation, 199
Aortography, present status of (abs), 132
Apical form of bronchopulmonary cancer, 457
Appendix, copraliths, surgical importance (abs), 432
mucocele of, roentgen features of (abs), 278
roentgen diagnosis of calculi of (abs), 432
Arachnodactyly, two case reports with etiological implications, 797
Arteriography, cerebral, in subarachnoid hemorrhage (abs), 426
of limbs (abs), 438
technical aspects of (abs), 869
Arthritis, chronic, roentgen diagnostic aspects of (abs), 436
rheumatoid, heart in (abs), 733
roentgen therapy in (abs), 583
Articulation, bilateral posttraumatic ulnocuneiform, 80
Atresia, congenital, and tracheoesophageal fistula (abs), 123
congenital, of foramina of Luschka and Magendie (abs), 263
congenital, of intestine and colon (abs), 130
Atrium, left, calcification in, in rheumatic heart disease, 202
Atrophy, familial osseous (abs), 281
Azygos lobe, its involvement in pulmonary disease, 195

Back, low, "last-straw" factor in disability of (abs), 869
Bacteria, studies on metabolism of radioisotopes by, 839
Bagasse disease of lungs (abs), 578
Banti's syndrome (abs), 433
Bartholin's glands, radium therapy for carcinoma of 517
Bartonella-infected rats, effect of roentgen rays upon, 95
BCG vaccination in all age groups (abs), 428
Bellevue Hospital, twenty-fifth anniversary of Radiation Therapy Department of, 571
Beryllium window roentgen tubes, high-intensity radiation from (abs), 589
Besnier-Boeck disease with transition into miliary tuberculosis (abs), 580
Beta irradiation, total surface, effects of (abs), 585
Betatron, techniques for application of, to medical therapy, 591
Biliary-bronchial fistula. traumatic (abs), 123
regurgitation, cholangiography and (abs), 279
Biological action of fast neutrons using summation method for lethal effects in mice, experiments on mechanism of (abs), 287
bases of associated action of hormones and roentgen rays on cancer cells of certain glands under hormonal control (abs), 588
significance of fibrinous radiomucositis of larynx (abs), 582
Blood of dogs, anticoagulant in, with hemorrhaagic tendency after total body exposure to roentgen rays (abs), 885
Boeck's disease and occurrence of minute mineral particles (abs), 579
disease, Kveim reaction in (abs), 579

disease with transition into miliary tuberculosis (abs), 580
sarcoid, progressive, associated with protracted destructive tuberculosis (abs), 580
BONE density, quantitative evaluation of, 808
giant cell tumors of (abs), 873
infection, chronic salmonella (abs), 434
lesions, erosive, associated with spinal cord injuries (abs), 434
measurement, method of determining by spot scanography, 402
metastases, occult (abs), 137
sclerosis in leukemia and in non-leukemic myelosis, 61
tumors, experiences with (abs), 136
BONES, long, in infants, double contour, cupping and spurring in roentgenograms of, 482
sesamoid, of hands and feet, 493
BOOK REVIEWS
Arthritis and Related Conditions. Edited by Theodore Franklin Bach, 421
Essentials of Pathology. By Lawrence W. Smith and Edwin S. Gault, 422
A Symposium on the Use of Isotopes in Biology and Medicine, 422
The Treatment of Malignant Disease by Radium and X-Rays: Being a Practice of Radiotherapy. By Ralston Paterson, 863
Radon: Its Technique and Use. By W. A. Jennings and S. Russ, 863
Standards for the Diagnosis and Treatment of Cancer. By the Cancer Committee of the Iowa Medical Society, 864
The Thyroid and Its Diseases. By J. H. Means, 864
BRAIN stem, upward transtentorial herniation of, due to tumor of posterior fossa (abs), 264
BREAST, female, effect of estrogenic hormone on advanced carcinoma of (abs), 286
technique of simple roentgenography of (abs), 439
BRONCHI, adenoma of, without signs of bronchial obstruction, 209
BRONCHIAL secretions, cancer cells in (abs), 120
tree, practical technique for visualization of (abs), 272
BRONCHIECTASIS, and esophagobronchial fistula of entire right lung (abs), 427
simulating chronic bronchitis (abs), 120
BRONCHIOGENIC carcinoma (abs), 271
BRONCHITIS, chronic, bronchiectasis simulating (abs), 120
BRONCHOGENIC carcinoma, early clinical features of (abs), 120
carcinoma, emphysema an early roentgen sign of (abs), 576
carcinoma, pulmonary tuberculosis simulating (abs), 577
BRONCHOGRAPHY in adults, technique of, 243
BRONCHOPULMONARY cancer, apical form of, 457
BRONCHOSPIROMETRIC findings, discrepancies between clinical-radiological and (abs), 733
BROOKHAVEN NATIONAL LABORATORY nuclear reactor, 570
BRUCELLOSIS, treatment of, by total teleroentgen therapy (abs), 873
BURSITIS, roentgen diagnostic aspects of (abs), 436
roentgen therapy in (abs), 583

CALCAREOUS peritendinitis, occupational, of feet, 506
CALCIFICATION, left atrial, in rheumatic heart disease, 202
of pleura and lung (abs), 428
pancreatic (abs), 739
symmetrical, of cerebral basal ganglia (abs), 741
CALCULI, appendiceal, roentgen diagnosis of (abs), 432
CALIBRATION, thimble chamber, on soft roentgen rays, 543
CANCER, bronchopulmonary, apical form of, 457
cells in bronchial secretions (abs), 120
cells of certain glands under hormonal control, biological bases of associated action of hormones and roentgen rays on (abs), 588
of female pelvis, intravaginal roentgen therapy of (abs), 874
of prostate (abs), 876
of stomach, mass roentgen survey of gastrointestinal tract to detect, 470
principles of fast electron therapy in, 232
problems of acquired radioresistance of (abs), 442
research, availability of radioisotopes free of production costs for, 729
role of hyaluronidase in invasiveness of (E), 405
Teaching Day, 420, 861
CARCINOGENIC properties of radioactive fission products and of plutonium (abs), 880
CARCINOMA, advanced, of female breast, effect of estrogenic hormone on (abs), 286
bronchiogenic (abs), 271
bronchogenic, early clinical features of (abs), 120
bronchogenic, emphysema an early roentgen sign of (abs), 576
bronchogenic, possibilities of roentgen diagnosis of, 753
bronchogenic, pulmonary tuberculosis simulating (abs), 577
cervical, late recurrence of, following radiation therapy (abs), 877
cutaneous, involving cartilage, roentgen treatment of, 380
effect of urethane on (abs), 286
gastric, cytologic method as aid in diagnosis of (abs), 734
gastric, detection of, by photofluorographic methods, 183, 188
human, quantitative histological analysis of radiation effects in (abs), 288

laryngeal, reactions of connective tissues after protracted fractionated irradiation of (abs), 582
of Bartholin's gland, radium therapy for, 517
of bowel, prognosis in (abs), 739
of cervix, improved methods of intravaginal roentgen and radium therapy in (abs), 875
of cervix, interstitial radium therapy in (abs), 875
of cervix, transvaginal roentgen therapy in (abs), 875
of cervix uteri, clinical diagnosis of (abs), 740
of cervix uteri, pathologic aspects of (abs), 741
of cervix uteri, physical aspects of intracavitary radium treatment of (abs), 877
of cervix uteri, role of transvaginal roentgen therapy in treatment of (abs), 285
of cervix uteri, surgical aspects of (abs), 741
of colon, gastrocolic fistula complicating (abs), 278
of lip, review of 563 cases (abs), 283
of pancreas, diagnostic criteria (abs), 432
of prostate, effects of estrogenic therapy on osseous metastases from (abs), 584
of prostate, life expectancy in (abs), 134
of rectum, relation of rectal polyps to (abs), 125
of skin, influence of dosage on success of treatment (abs), 583
of stomach (abs), 124
of tonsil (abs), 582
of transverse colon in boy (abs), 431
of uterine cervix, five year end results in treatment of (abs), 875
of uterine cervix, intracavitary radium therapy of (abs), 874
of uterine cervix, late results of radium therapy for (abs), 878
primary papillary, of ureter (abs), 132
primary sensory neuropathy with muscular changes associated with (abs), 281
simulating pulmonary tuberculosis (abs) 576
CARCINOSARCOMA of esophagus, 461
CARDIO-ESOPHAGEAL relaxation as cause of vomiting in infants (abs), 266
CARTILAGE, cutaneous carcinoma involving, roentgen treatment of, 380
CARTILAGINOUS tumors of hand (abs), 139
CASSETTE, grid-front (abs), 881
CATHETERIZATION, venous, of heart (abs), 273
CAVITIES, infected, demonstration of, by lipiodol, 223
CELLS, malignant, quantitative analysis of direct and indirect action of roentgen radiation on (abs), 287
CEPHALOPELVIMETRY (abs), 279
CEREBELLUM, upward transtentorial herniation of, due to tumor of posterior fossa (abs), 264
CEREBRAL angiography, technical improvements in (abs), 426
arteriography in subarachnoid hemorrhage (abs), 426
tumors, experimental, irradiation of (abs), 585
CERVICAL disc, minor fractures of cervical laminae simulating ruptured (abs), 267
injuries, hyperextension, with normal roentgen appearances, paraplegia in (abs), 142
CERVIX UTERI, carcinoma, role of transvaginal roentgen therapy in treatment of (abs), 285
clinical diagnosis of carcinoma of (abs), 740
five year end results in treatment of carcinoma of (abs), 875
improved methods of intravaginal roentgen and radium therapy in carcinoma of (abs), 875
interstitial radium therapy in carcinoma of (abs), 875
intracavitary radium therapy for carcinoma of (abs), 874
late recurrence of carcinoma of, following radiation therapy (abs), 877
late results of radium therapy for carcinoma of (abs), 878
pathologic aspects of carcinoma of (abs), 741
physical aspects of intracavitary radium treatment of carcinoma of (abs), 877
surgical aspects of carcinoma of (abs), 741
transvaginal roentgen therapy in carcinoma of (abs), 875
CHEST, children's, interpretation of roentgenograms of (abs), 121
lateral tomogram of, in normal subject (abs), 428
surveys, mass, medical and roentgenological aspects of, 147
CHILDREN, fractures of lower end of humerus in (abs), 138
interpretation of roentgenograms of chest of (abs), 121
roentgen treatment of infections of tonsils and post-pharyngeal lymphoid tissues in (abs), 438
uptake of radioactive iodine by normal and disordered thyroid gland in (abs), 574
CHLOROMA, unusual roentgen shadow in (abs), 436
CHOLANGIOGRAPHY and biliary regurgitation (abs), 279
CHOLECYSTOGRAPHY, comparative study of oral and intravenous contrast substances (abs), 278
CIRCULATION, lesser, anatomy and physiology of, as indicated by its behavior in health and disease, 1
lesser, conditions which result in increased pressure within, 26
lesser, evaluation of, as portrayed by the roentgenogram, 30
CITIES, small, part time radiological practice in hospitals of, 236
CLIP DRIP TRAY, new processing room accessory, 100
CLOSTRIDIAL infections in dogs, experimental (abs), 584

COARCTATION, aortic aneurysm secondary to (abs), 275
of aorta, surgical treatment for (abs), 123
occurrence and diagnosis of dilatation of aorta distal to area of, 199
COCCIDIOIDOMYCOSIS, early, roentgen findings in (abs), 270
COLCHICINE, effects of, on cornea (abs), 875
COLE, WILLIAM GREGORY, 1902–1948, obituary, 252, portrait, 252
COLON, atony of, investigation of (abs), 130
congenital atresia of (abs), 130
congenitally small (abs), 738
gastrocolic fistula complicating carcinoma of (abs), 278
malrotation of (abs), 130
prognosis in carcinoma of (abs), 739
transverse, carcinoma of, in boy (abs), 431
CONDYLES, tibial, fractures of, involving knee joint (abs), 868
CONES, malleable, for roentgen therapy, 245
CONFERENCE of health officers and public health nurses, 420
CONGENITAL absence of humeral head (abs), 138
atresia and tracheoesophageal fistula (abs), 123
atresia of foramina of Luschka and Magendie (abs), 263
atresia of intestine and colon (abs), 130
coxa vara, treatment of (abs), 144
dislocation of hip in infancy, results of treatment of (abs), 145
duodenal obstruction (abs), 430
hydronephrosis and hydroureter (abs), 133
hypertrophic stenosis, pyloric spasm simulating (abs), 124
pneumonitis in newborn infants (abs), 578
pulmonary stenosis (abs), 122
CONNECTIVE tissues, reactions of, after protracted fractionated irradiation of laryngeal carcinoma (abs), 582
CONTRAST media for roentgenographic diagnosis iodinated organic compounds as (abs), 586
substances, comparative study of oral and intravenous, for cholecystography (abs), 278
CONVOLUTIONAL markings in skull roentgenograms of patients with headache, 317
COPRALITHS, appendiceal, surgical importance (abs), 432
CORNEA, comparison of effects of mustard, ultraviolet and roentgen radiation, and cholchicine on (abs), 875
COXA VARA, congenital, treatment of (abs), 144
CRERAR LIBRARY, private library of Emil H. Grubbe given to, 730
CYSTS, pericardial celomic (abs), 272
peripelvic lymphatic, of kidney (abs), 433
pulmonary, in infant, lobectomy for (abs), 427
CYTOLOGIC method as aid in diagnosis of gastric carcinoma (abs), 734
DACTYLITIS, tuberculous, in adult (abs), 140
DAVID ANDERSON-BERRY prize, 571
DEFICIENCY diseases, small intestinal pattern in, 658
DELANO, PERCY JOSEPH, 1899–1949, obituary, 854
portrait, 854
DESOXYCORTICOSTERONE ACETATE, treatment of radiation sickness with, 387
DIAPHRAGM, various types of hernia of, treated surgically (abs), 126
DIODRAST, spinal extradural hemangioblastoma roentgenographically visualized by, at operation (abs), 742
DISLOCATION, congenital, of hip in infancy, results of treatment of (abs), 145
of hip, lateral view of pelvis in examination for (abs), 146
of pisiform (abs), 137
DIVERTICULA of foregut (abs), 738
DIVERTICULUM, duodenal, benign ulceration within (abs), 430
intraluminal, producing intermittent duodenal obstruction or stasis, 212
of Meckel, patent omphalomesenteric duct and its relation to (abs), 128
DOGS, experimental clostridial infections in (abs), 584
DOSAGE calculations for various plans of intravaginal therapy (abs), 876
influence of, on success of treatment of carcinoma of skin (abs), 583
rate meter, negative feedback, using very small ionization chamber, 550
DOSES, repeated low, of neutrons, effects of, on estrous cycle of white rat, 530
DRUGS, pharmacological reactions of, irradiated with roentgen rays of varying wavelength, 534
DUODENAL mechanism regulating motor and secretory activity of stomach (abs), 277
ulcer, roentgenographic disturbance of duodenal mechanism regulating motor and secretory activity of stomach (abs), 277
DUODENUM, benign ulceration within diverticulum of (abs), 430
congenital obstruction of (abs), 430
intraluminal diverticulum and other lesions producing intermittent obstruction or stasis of, 212
regurgitation of (abs), 128
retroperitoneal perforation of (abs), 430
DYSPLASIA, monostotic fibrous, 354

EASTERN CONFERENCE OF RADIOLOGISTS, 114
EDEMA, pulmonary, possibilities of roentgen diagnosis of, 745
EDITORIALS
Nitrogen mustard therapy, 104
Eldwin R. Witwer, 1890–1948, 108
José Francisco Merlo Gómez, 110
Legg-Perthes' disease, 248
Hirschsprung's disease, 250

William Gregory Cole, 1902–1948, 252
The clinical and roentgenological implications of hyaluronidase, 405
Gordon E. Richards, 1885–1949, 409
René Ledoux-Lebard, 1879–1948, 412
Frank Edward Simpson, 1868–1948, 415
Gastric vascular shunts, 561
Radiation hygiene, 718
Jeremiah Fletcher Lutz, 1872–1948, 719
Robert Earl Pound, 1893–1949, 721
Intussusception, 851
Thomas S. Stewart, 1876–1949, 853
Percy Joseph Delano, 1899–1949, 854
Effects, biological, of pile radiations (abs), 879
early, of roentgen rays on ovaries of rat (abs), 586
hematological, of ionizing radiations in tolerance range (abs), 590
of repeated low doses of neutrons on estrous cycle of white rat, 530
of total surface beta irradiation (abs), 585
physiological, of ionizing radiation in animals, clinical sequence of (abs), 882
Effusion, pericarditis with, value of angiocardiography in establishing diagnosis of, 41
Electron therapy in cancer, principles of, 232
Electroshock therapy, fractures following (abs), 438
Elements, heaviest, metabolism of fission products and (abs), 587
Emphysema, early roentgen sign of bronchogenic carcinoma (abs), 576
Endometriosis as cause of intestinal obstruction (abs), 735
Enteritis, cicatrizing, 366
Enterogastrone, treatment of peptic ulcer with (abs), 734
Enzymes, effect of nitrogen mustards on (abs), 884
Epipericardial fat shadows in differential diagnosis (abs), 274
Epiphysis, treatment of slipped capital femoral (abs), 434
Epithelioma, extensive, of larynx, roentgen treatment for, 260
of eyelids, treatment of (abs), 872
of skin, treatment of (abs), 871
Erthroblastosis fetalis, clinical and roentgen manifestations of, 291
Esophagitis (abs), 573
Esophagus, carcinosarcoma of, 461
surgical management of acquired stricture of (abs), 427
Estrogenic hormone, effect of, on advanced carcinoma of female breast (abs), 286
therapy, effects of, on osseous metastases from carcinoma of prostate (abs), 584
Estrous cycle of white rat, effects of repeated low doses of neutrons on, 530
Eyelids, treatment of epithelioma of (abs), 872
Facsimile, roentgenographic, 557
Familial osseous atrophy (abs), 281
Fat shadows, epipericardial, in differential diagnosis (abs), 274
Fatigue fractures of fibula (abs), 141
Feet, occupational calcareous peritendinitis of, 506
sesamoid bones of, 493
Femur, treatment of slipped capital epiphysis of (abs), 434
Fibrin film in neurosurgery (abs), 263
Fibrosarcoma, synovial (abs), 867
Fibula, fatigue fractures of (abs), 141
Fission products, metabolism of, and heaviest elements (abs), 587
Fistula, esophagobronchial, and bronchiectasis of entire right lung (abs), 427
gastrocolic, complicating carcinoma of colon (abs), 278
neonatal gastrocolic (abs), 124
recto-urethral (abs), 432
tracheoesophageal, and congenital atresia (abs), 123
traumatic biliary-bronchial (abs), 123
Fistulas, demonstration of, by lipiodol, 223
Foramina of Luschka and Magendie, congenital atresia of (abs), 263
Foregut, diverticula of (abs), 738
Foreign body localization in soft parts (abs), 580
Fossa, posterior, upward transtentorial herniation of brain stem and cerebellum due to tumor of (abs), 264
Fracture, avulsion, of lesser tuberosity of humerus (abs), 139
of first rib (abs), 135
Fractures, fatigue, of fibula (abs), 141
following electroshock therapy (abs), 438
gunshot, of mandible (abs), 281
minor, of cervical laminae simulating ruptured cervical disc (abs), 267
of lower end of humerus in children (abs), 138
of tibial condyles involving knee joint (abs), 868
Fungi, studies on metabolism of radioisotopes by, 839

Gallbladder, classification of accessory, 671
double, 671
Ganglia, cerebral basal, symmetrical calcification of, 741
Gargoylism (abs), 870
Gastric secretion, effect of tetra-ethyl ammonium chloride on (abs), 127
vascular shunts (E), 561
Gastrocolic fistula, neonatal (abs), 124
Gastroenterology, recent advances in treatment in field of (abs), 429
Gastrointestinal tract, chronic granulomas in, caused by minute mineral particles (abs), 579

mass roentgen survey of, to detect cancer of stomach, 470
roentgenographic studies of, following section of vagus nerves for peptic ulcer (abs), 124
GLASSES, trifocal, as aid to older roentgenologist, 102
GLIOBLASTOMA, case of, treated by betatron, 591
GÓMEZ, JOSE FRANCISCO MERLO, obituary, 110
GONADOTROPIC function of hypophysis of mature and immature female albino rat, effect of low dosage roentgen radiation on (abs), 884
GOUT, clinical, pathological and roentgenographic observations (abs), 435
report of unusual case in young man (abs), 140
GRANULOMAS, chronic, in alimentary tract caused by minute mineral particles (abs), 579
GRUBBE, EMIL H., private library of, given to John Crerar Library, 730

HAND, cartilaginous tumors of (abs), 139
HANDS, sesamoid bones of, 493
HEADACHE, convolutional markings in skull roentgenograms of patients with, 317
HEART disease, rheumatic, left atrial calcification in, 202
enlargement of (abs), 275
in rheumatoid arthritis (abs), 733
rheumatic mitral valve disease without enlargement of (abs), 275
roentgen kymographic study of, in myasthenia gravis (abs), 274
simple procedure for evaluation of mobility of (abs), 732
venous catheterization of (abs), 273
HEMANGIOBLASTOMA, spinal extradural, roentgenographically visualized with diodrast at operation and successfully removed (abs), 742
HEMANGIO-ENDOTHELIOMA, skeletal (abs), 134
HEMANGIOLIPOMA, extradural, Klippel-Feil's syndrome associated with compression of spinal cord by (abs), 267
HEMANGIOMA of small intestine, with special reference to intussusception (abs), 125
primary, of skull, rare cranial tumor, 302
HEMATOLOGICAL effects of ionizing radiations in tolerance range (abs), 590
HEMATOMA, subdural (abs), 426
HEMATOMAS, association of certain, with myelencephalic blebs in house mouse, 98
HEMORRHAGE, subarachnoid, cerebral arteriography in (abs), 426
subepithelial, of renal pelvis simulating neoplasm (abs), 131
HEMORRHAGIC tendency in congestive splenomegaly (abs), 433
HEMOSIDEROSIS of lung due to mitral disease, 443
HERNIA, diaphragmatic, various types of, treated surgically (abs), 126
HERNIATION of nucleus pulposus, complete block of lumbar spinal canal due to, 775
upward transtentorial, of brain stem and cerebellum due to tumor of posterior fossa (abs), 264
HIP, congenital dislocation of, in infancy, results of treatment of (abs), 145
dislocation, lateral view of pelvis in examination for (abs), 146
HIRSCHSPRUNG'S DISEASE (E), 250
HISTOLOGICAL changes following radiation exposures (abs), 885
HN_2, role of, as systemic adjunct to radiation therapy of certain malignant diseases, 626
HODGKIN'S DISEASE, histopathological and clinical classification with radiotherapeutic response, 369
roentgen therapy in (abs), 440
HORMONE, adrenal cortical, treatment of radiation sickness with, 387
HORMONES and roentgen rays, biological bases of associated action of, on cancer cells of certain glands under hormonal control (abs), 588
HOSPITALS, Alabama State, tuberculosis in (abs), 575
of small cities, part time radiological practice in, 236
HUMERAL head, congenital absence of (abs), 138
HUMERUS, avulsion fracture of lesser tuberosity of (abs), 139
fractures of lower end of, in children (abs), 138
HYALURONIDASE, clinical and roentgenological implications of (E), 405
effect of, on absorption of subcutaneously deposited radiopaque substance, 91
HYDRONEPHROSIS, congenital (abs), 133
HYDROURETER, congenital (abs), 133
HYPERTENSION, pulmonary, causes of, 27
HYPOPHYSIS of mature and immature female albino rat, effect of low dosage roentgen radiation on gonadotropic function of (abs), 884

ILEITIS, regional, of prenatal origin, 366
ILEUS, atypical adynamic, apparently caused by nutritional deficiency (abs), 131
INFANT, lobectomy for pulmonary cysts in (abs), 427
INFANTS, cardio-esophageal relaxation as cause of vomiting in (abs), 266
double contour, cupping and spurring in roentgenograms of long bones in, 482
malignant melanoma in (abs), 281
newborn, congenital pneumonitis in (abs), 578
results of treatment of congenital dislocation of hip in (abs), 145
INJURIES, prevention of, caused by ionizing radiations (abs), 289
INNOMINATE artery, anomalous, compression of trachea by (abs), 573
INSTRUCTION COURSES at Cincinnati meeting, 731

Inter-American Congress of Radiology, Third, 116, 257, 420, 860
International Congress of Radiology, Sixth, 257, 420
Intervertebral disc, herniated (abs), 143
protrusion, lumbar, contralateral to side of symptoms and signs, 77
ruptured, in cervical region (abs), 143
Intestine, acute obstruction of, in typhoid fever (abs), 125
congenital atresia of (abs), 130
dyskinesia of, investigation of (abs), 130
endometriosis as cause of obstruction of (abs), 735
role of radiologist in management of patients with obstruction of (abs), 736
small, acute obstruction of (abs), 736
small, hemangioma of, with special reference to intussusception (abs), 125
small, malignant tumors of (abs), 738
small, pattern of, in sprue and similar deficiency diseases, 658
small, primary nonspecific ulcers of (abs), 431
small, rapid method of roentgen examination of, 45
small, roentgenologic study of (abs), 735
small, rupture of, complicating injury of pelvis (abs), 431
Intracranial angiography, practical serialograph for, 324
mass lesions, roentgen findings in, 762
neoplasms, differential diagnosis of, by cerebral angiography (abs), 265
tuberculomas, calcified (abs), 262
Intravaginal therapy, dosage calculations for various plans of (abs), 876
Intussusception (E), 851
hemangioma of small intestine, with special reference to (abs), 125
Inverse square law, application of, to oil immersed tubes (abs), 588
Iodinated organic compounds as contrast media for roentgenographic diagnoses (abs), 586
Ionization chamber, very small, negative feedback dosage rate meter using, 550
Ionizing radiation in animals, clinical sequence of physiological effects of (abs), 882
radiations in tolerance range, hematological effects of (abs), 590
Irradiation, beta, effects of total surface (abs), 585
of experimental cerebral tumors (abs), 585
protracted fractionated, of laryngeal carcinoma, reactions of connective tissues after (abs), 582
spray, treatment of polycythemia by (abs), 284
Isotopes and radiation hazards (abs), 288
in clinical and experimental medicine (abs), 879
radioactive, study of peripheral vascular disease with (abs), 289
use of, in surgical research (abs), 288

Jejunum, adenocarcinoma of, 680

Kaposi's sarcoma, 511
Keloids, treatment of (abs), 872
Kidney pelvis, subepithelial hemorrhage of, simulating neoplasm (abs), 131
peripelvic lymphatic cysts of (abs), 433
Klippel-Feil's syndrome associated with compression of spinal cord by extradural hemangiolipoma (abs), 267
Knee joint, fractures of tibial condyles involving (abs), 868
roentgen diagnosis of pigmented villonodular synovitis and synovial sarcoma of (abs), 435
Kveim reaction in Boeck's disease (abs), 579

Laminae, cervical, minor fractures of, simulating ruptured cervical disc (abs), 267
Larynx, biological significance of fibrinous radiomucositis of (abs), 582
irradiated, late changes in mucous membrane of (abs), 439
reactions of connective tissues after protracted fractionated irradiation of carcinoma of (abs), 582
roentgen treatment for extensive epithelioma of, 260
Latex cap for radon ointment treatment (abs), 584
Ledoux-Lebard, René, 1879–1948, medal of, 414
obituary, 412
portrait, 412
Legg-Perthes' disease (E), 248
Letterer-Siwe disease (abs), 868
Leucoderma, treatment of (abs), 872
Leukemia, bone sclerosis in, 61
chronic myelogenous (abs), 873
effect of urethane on (abs), 286
Leukemias (abs), 581
Limbs, arteriography of (abs), 438
Lip, carcinoma, review of 563 cases (abs), 283
Lipiodol, demonstration of sinus tracts, fistulas and infected cavities by, 223
Lipochondrodystrophy (abs), 870
Liver, adrenal tumor of, in child (abs), 432
anomalous lobe of, 258, 260
Lobectomy for pulmonary cysts in infant (abs), 427
Localization, foreign body, in soft parts (abs), 580
Los Angeles Radiological Society, 260
Lung, calcification of (abs), 428
entire right, esophagobronchial fistula and bronchiectasis of (abs), 427
hemosiderosis of, due to mitral disease, 443
vascular structure of, 5
Lungs, absorption of radon through skin and exhalation through (abs), 589
amebiasis with involvement of (abs), 122
bagasse disease of (abs), 578
congenital stenosis of (abs), 122
function of, 23

function of, following pneumothorax (abs), 577
involvement of azygos lobe in disease of, 195
lobectomy for cysts in, in infant (abs), 427
metastasis to, possibilities of roentgen diagnosis, 751
peripheral vascular disease in, 17
sarcoidosis of, early roentgen findings (abs), 268
Lutz, Jeremiah Fletcher, 1872–1948, obituary, 719
portrait, 719
Lymphoblastoma, evaluation of differences in sensitivity to roentgen irradiation of different types (abs), 439
Lymphomas (abs), 581

Malignant disease, effect of urethane on (abs), 286
diseases, nitrogen mustard as systemic adjunct to radiation therapy of, 626
growth, relation between radiation effects, cell viability and induced resistance to (abs), 881
Malrotation of colon (abs), 130
Mandible, gunshot fractures of (abs), 281
Marfan's syndrome, 797
Measurement, bone, method of determining, by spot scanography, 402
depth dose, for 250 kv. roentgen rays, 397
Measurements, low-absorption roentgen-ray, from 500 to 1,000 kilovolts (abs), 588
Mechanism of biological action of fast neutrons using summation method for lethal effects in mice (abs), 287
Medical therapy, techniques for application of betatron to, 591
Medicine, clinical and experimental, isotopes in (abs), 879
Melanoma, malignant, in infancy (abs), 281
prepubertal, of skin (abs), 870
Melorheostosis, interesting case of (abs), 135
Meningiomas, spinal, diagnosis of, by myelography, 683
Meningocele, intrathoracic, Recklinghausen's neurofibromatosis associated with (abs), 742
Metabolism of fission products and heaviest elements (abs), 587
of radioisotopes, studies on, by various fungi and bacteria, 839
tissue, effect of nitrogen mustards on (abs), 884
Metastases, occult bone (abs), 137
osseous, from carcinoma of prostate, effects of estrogenic therapy on (abs), 584
Metastasis to lungs, possibilities of roentgen diagnosis of, 751
Microarteriography (abs), 883
Microcolon (abs), 738
Microroentgenography, medical, biological and industrial applications of (abs), 881
Miller-Abbott tube, use of, in patients with intestinal obstruction (abs), 736
Mineral particles, minute, chronic granulomas in alimentary tract caused by (abs), 579
Mitral disease, hemosiderosis of lung due to, 443
valve disease, rheumatic, without cardiac enlargement (abs), 275
Mouse, association of certain hematomas with myelencephalic blebs in, 98
Mucocele of appendix, roentgen features of (abs), 278
Mucosa, prolapsed gastric, roentgen diagnosis of, 784
Mucosal deformities of greater curvature of stomach (abs), 429
Mucous membrane of irradiated larynx, late changes in (abs), 439
Mumps, roentgen manifestations of pancreatitis complicating, 219
Muscular changes, primary sensory neuropathy with, associated with carcinoma (abs), 281
Mustard, effect of, on cornea (abs), 875
nitrogen, effect of, on enzymes and tissue metabolism (abs), 884
nitrogen, role of, as systemic adjunct to radiation therapy of certain malignant diseases, 626
nitrogen, therapy (E), 104
Myasthenia gravis, roentgen kymographic study of heart in (abs), 274
Myelencephalic blebs in house mouse, association of certain hematomas with, 98
Myelography, diagnosis of spinal meningiomas and schwannomas by, 683
discrepancies in (abs), 280
pantopaque (abs), 280
value of, in lumbar discogenic disease, 77
Myelosis, non-leukemic, bone sclerosis in, 61
Myositis ossificans, traumatic, roentgen therapy in (abs), 284

Necrosis, radiation (abs), 282
Neoplasm, primary benign, of ureter (abs), 133
subepithelial hemorrhage of renal pelvis simulating (abs), 131
Neoplasms, intracranial, differential diagnosis of, by cerebral angiography (abs), 265
Nerves, vagus, roentgenographic studies of gastrointestinal tract following section of, for peptic ulcer (abs), 124
Neuroarthropathy, paraplegic, 475
Neuroblastoma (abs), 129
Neurofibroma of prostate gland (abs), 133
Neurofibromatosis, Recklinghausen's, associated with intrathoracic meningocele (abs), 742
Neuropathy, primary sensory, with muscular changes associated with carcinoma (abs), 281
Neurosurgery, fibrin film in (abs), 263
Neutrons, effects of repeated low doses of, on estrous cycle of white rat, 530
fast, experiments on mechanism of biological

action of, using summation method for lethal effects in mice (abs), 287
Nuclear reactor at Brookhaven National Laboratory, 570
Nucleus pulposus, complete block of lumbar spinal canal due to herniation of, 775
Nutritional deficiency, atypical adynamic ileus apparently caused by (abs), 131

Obstruction, acute, of small bowel (abs), 736
congenital duodenal (abs), 430
intestinal, endometriosis as cause of (abs), 735
role of radiologist in management of patients with (abs), 736
Omphalomesenteric duct, patent, and its relation to diverticulum of Meckel (abs), 128
Oncology, course on, 862
Osgood-Schlatter disease (abs), 867
Osseous atrophy, familial (abs), 281
metastases from carcinoma of prostate, effects of estrogenic therapy on (abs), 584
Ossification centers, unfused, associated with pain in the adult, 341
Ossifications, soft tissue, associated with spinal cord injuries (abs), 434
Osteochondritis dissecans of ankle (abs), 435
of spine, etiology of (abs), 868
Osteogenesis imperfecta tarda, 690
Osteopetrosis (abs), 134
Ovarian pain and insufficiency, syndrome of (abs), 741
tissue, importance of conserving (abs), 741
Ovaries of rat, early effects of roentgen rays on (abs), 586

Pain, unfused ossification centers associated with, in adult, 341
Palate, mixed tumors of, 82
Pancoast Lecture, 1947, 743
Pancreas, calcification of (abs), 739
diagnostic criteria of carcinoma of (abs), 432
Pancreatitis, complicating mumps, roentgen manifestations of, 219
Pantopaque myelography, statistical survey of 200 operative cases undergoing (abs), 280
Paraplegia in cervical spine injuries (abs), 142
in hyperextension cervical injuries with normal roentgen appearances (abs), 142
Paraplegic neuroarthropathy, 475
Pelvimetry, roentgen, elastic ruler for (abs), 584
Pelvis, female, intravaginal roentgen therapy of cancer of (abs), 874
lateral view of, in examination for hip dislocation (abs), 146
rupture of small complicating injury of (abs), 431
Pennsylvania Radiological Society, 420
Peptic ulcer, co-existent benign, and adenocarcinoma of stomach, 677
effect of tetra-ethyl ammonium chloride on acidity in (abs), 127
produced experimentally by vascular ligation (abs), 127
roentgenographic studies of gastrointestinal tract following section of vagus nerves for (abs), 124
treatment of, with enterogastrone (abs), 734
vagotomy in treatment of (abs), 126; (abs), 127
Pericardial celomic cysts (abs), 272
Pericarditis with effusion, value of angiocardiography in establishing diagnosis of, 41
Peripheral vascular disease in lungs, 17
Peritendinitis, occupational calcareous, of feet, 506
Pharmacological reactions of sera and drugs irradiated with roentgen rays of varying wavelength, 534
Photofluorographic methods, detection of gastric carcinoma by, 183, 188
Physicists, radiation, certification of, by American Board of Radiology, 116
Physics, modern, symposium on, 862
Physiology of lesser circulation, indicated by its behavior in health and disease, 1
Pisiform, dislocation of (abs), 137
Pleura, calcification of (abs), 428
Pleural effusion, possibilities of roentgen diagnosis of, 747
Plutonium, carcinogenic properties of (abs), 880
Pneumocholecystitis, acute (abs), 128
Pneumoconiosis, hemosiderosis of lung due to mitral disease simulating, 443
Pneumonia associated with acute salmonellosis (abs), 577
possibilities of roentgen diagnosis of, 747
rheumatic (abs), 268
unresolved, an exclusion diagnosis, 335
Pneumonitis, congenital, in newborn infants (abs), 578
Pneumothorax, pulmonary function following (abs), 577
Polycythemia vera, treatment of, by spray irradiation (abs), 284
Polyps, rectal (abs), 125
Pound, Robert Earl, 1893–1949, obituary, 721
portrait, 721
Prenatal origin, regional ileitis of, 366
Processing room accessory, new—clip drip tray, 100
Projector, portable, for roentgenograms, 847
Prostate gland, cancer of (abs), 876
carcinoma of, life expectancy in (abs), 134
effects of estrogenic therapy on osseous metastases from carcinoma of (abs), 584
giant, without symptoms (abs), 133
Pseudarthrosis in lumbosacral spine (abs), 144
Pyelography, intravenous, range of usefulness of (abs), 279
Pylorus, spasm of, simulating congenital hypertrophic stenosis (abs), 124
Pyuria, sterile, 711

RADIATION, cross, simultaneous (abs), 580
doses received by skin of patient during routine diagnostic roentgen examination (abs), 286
effects in human carcinomas, quantitative histological analysis of (abs), 288
exposures, histological changes following (abs), 885
hazards from isotopes (abs), 288
high-intensity, from beryllium window roentgen tubes (abs), 589
hygiene (E), 718; 726
necrosis (abs), 282
parasitic, study of quality and origin of, from target of roentgen tube (abs), 589
protection, use for, of gloves laden with thorium oxide (abs), 884
sickness, treatment of, with adrenal cortical hormone, 387
Therapy Department of Bellevue Hospital, twenty-fifth anniversary of, 571
therapy of malignant diseases, role of nitrogen mustard as systemic adjunct to, 626
RADIATIONS, ionizing, hematological effects of, in tolerance range (abs), 590
ionizing, tolerance dose and prevention of injuries caused by (abs), 289
pile, biological effects of (abs), 879
RADIOACTIVE decay, slide rule calculations of (abs), 880
fission products, carcinogenic properties of (abs), 880
iodide, accumulation of, by thyroid gland in normal and thyrotoxic subjects (abs), 881
iodine, uptake of, by normal and disordered thyroid gland in children (abs), 574
RADIOAUTOGRAPHS, preparation of, of thyroid tumors, for study at high magnification (abs), 574
RADIOIODINE, distribution in animal body of organisms containing, 839
in therapy and diagnosis (abs), 879
partial destruction of rat thyroid by large doses of, 731
RADIOISOTOPES as tracers, basic courses in techniques of using, 570
availability of, free of production costs for cancer research, 729
studies on metabolism of, by various fungi and bacteria, 839
RADIOLOGICAL practice, part time, in hospitals of small cities, 236
RADIOLOGIST, role of, in management of patients with intestinal obstruction (abs), 736
RADIOLOGISTS, Eastern Conference of, 114
RADIOLOGY, inspection of training facilities in, by American Board of Radiology, 728
Sixth International Congress of, 257, 420
Third Inter-American Congress of, 116, 257, 420, 860
RADIOMUCOSITIS, fibrinous, of larynx, biological significance of (abs), 582
RADIOPAQUE sponges, roentgen recognition of, 706
substance, subcutaneously deposited, effect of hyaluronidase on absorption of, 91
RADIOPHOSPHORUS in therapy and diagnosis (abs), 879
RADON, absorption of, through skin and its exhalation through lungs (abs), 589
ointment treatment, latex cap for (abs), 584
RAT, early effects of roentgen rays on ovaries of (abs), 586
white, effects of repeated low doses of neutrons on estrous cycle of, 530
RATS, effect of roentgen rays upon *Bartonella*-infected and normal, 95
RECTUM, carcinoma of, relation of rectal polyps to (abs), 125
polyps of (abs), 125
RESEARCH fellowships, American College of Physicians, 862
RESPIRATORY mechanics, studies on, 637
RETICULOENDOTHELIOSIS, systemic aleukemic (abs), 868
RETROGASTRIC soft tissues, midline, procurement and critical appraisal of width diameter of, 56
RHEUMATIC disease, pathology of (abs), 436
mitral valve disease without cardiac enlargement (abs), 275
pneumonia (abs), 268
RHEUMATOID arthritis, heart in (abs), 733
spondylitis (abs), 437
RHINOPHARYNX, roentgen diagnosis of malignant tumors of (abs), 427
RIB, first, fracture of (abs), 135
RIBONUCLEIC acid synthesis, inhibition of, in tumor tissue by irradiation with roentgen rays (abs), 885
RICHARDS, GORDON E., 1885–1949, obituary, 409
portrait, 409
ROCHESTER ROENTGEN RAY SOCIETY, 260
ROCKY MOUNTAIN RADIOLOGICAL SOCIETY, program of 1949 meeting, 859
ROENTGEN anatomy of oblique views of lumbar spine, 699
diagnosis, possibilities and limitations of, 743
examination of small intestine, rapid method of, 45
film, negative, method of roentgen-ray reproduction (abs), 881
kymographic study of heart in myasthenia gravis (abs), 274
pelvimetry, elastic ruler for (abs), 584
radiation, effects of, on cornea (abs), 875
radiation, low dosage, effect of, on gonadotropic function of hypophysis of mature and immature female albino rat (abs), 884
radiation, quantitative analysis of direct and indirect action of, on malignant cells (abs), 287

-ray measurements, low-absorption, from 500 to 1,000 kilovolts (abs), 588
-ray reproduction of negative roentgen film (abs), 881
rays and hormones, biological bases of associated action of, on cancer cells of certain glands under hormonal control (abs), 588
rays, anticoagulant in blood of dogs with hemorrhagic tendency after total body exposure to (abs), 885
rays, early effects of, on ovaries of rat (abs), 586
rays, effect of, upon *Bartonella*-infected and normal rats, 95
rays, high energy, appraisal of risks of, 592
rays, histological and histochemical study of skin of guinea pig treated with (abs), 886
rays of varying wavelength, pharmacological reactions of sera and drugs irradiated with, 534
rays, soft, thimble chamber calibration on, 543
rays, 250 kv., depth dose measurements for, 397
recognition of radiopaque sponges, 706
therapy, effect of, on tissue reactions to fibrin film (abs), 263
therapy, malleable cones for, 245
tube, study of quality and origin of parasitic radiation from target of (abs), 589
tubes, high-intensity radiation from beryllium window (abs), 589
tubes, oil-immersed, application of inverse square law to (abs), 588
ROENTGENOGRAMS, evaluation of lesser circulation as portrayed by, 30
of skull, convolutional markings in, of patients with headache, 317
portable projection for, 847
rapid accurate method for reproducing, at distance via wire or radio transmission, 577
stereoscopic, simple, inexpensive set of prisms for viewing, 715
ROENTGENOGRAPHIC diagnosis, iodinated organic compounds as contrast media for (abs), 586
facsimile, 557
ROENTGENOGRAPHY, monochromatic, medical, biological and industrial applications of (abs) 881
technique of simple breast (abs), 439
ROENTGENOLOGIST, older, trifocal glasses as aid to, 102
ROENTGENOLOGY, value of, in prognosis of minimal tuberculosis, 153
RULER, elastic, for roentgen pelvimetry (abs), 584
RUPTURE, spontaneous, of cerebral ventricles (abs), 264

SALMONELLA bone infection, chronic (abs), 434
SALMONELLOSIS, acute, pneumonia associated with (abs), 577
SAMUEL FREEDMAN LECTURES, 420
SARCOID (abs), 579
progressive Boeck's, associated with protracted destructive tuberculosis (abs), 580
SARCOIDOSIS (abs), 578
pulmonary, early roentgen findings (abs), 268
SARCOMA, Kaposi's, 511
of uterus, 830; (abs), 876
synovial, of knee joint, roentgen diagnosis (abs), 435
SCANOGRAPHY, spot, method of determining bone measurement, 402
SCHWANNOMAS, spinal, diagnosis of, by myelography, 683
SCLEROSIS, bone, in leukemia and in non-leukemic myelosis, 61
SEMILUNAR bone, unstable (abs), 137
SERA, pharmacological reactions of, irradiated with roentgen rays of varying wavelength, 534
SERIALOGRAPH, practical, for intracranial angiography, 324
SESAMOID bones of hands and feet, 493
SHOULDER, painful (abs), 137
SIDEROSIS, welders', clearing of roentgen shadows in (abs), 119
SIMPSON, FRANK EDWARD, 1868–1949, obituary 415
portrait, 415
SINUS tracts, demonstration of, by lipiodol, 223
SKELETON, hemangio-endothelioma of (abs), 134
SKIN, absorption of radon through, and exhalation through lungs (abs), 589
carcinoma, influence of dosage on success of treatment (abs), 583
of guinea pig treated with roentgen rays, histological and histochemical study of (abs), 886
prepubertal melanoma of (abs), 870
radiation doses received by, during routine diagnostic roentgen examination (abs), 286
treatment of epitheliomas of (abs), 871
SKULL, convolutional markings in roentgenograms of, of patients with headache, 317
primary hemangioma of, 302
SPINAL block, differential (abs), 130
canal, lumbar, complete block of, due to herniation of nucleus pulposus, 775
cord, compression of, by extradural hemangiolipoma, Klippel-Feil's syndrome associated with (abs), 267
cord, erosive bone lesions and soft tissue ossifications associated with injuries of (abs), 434
SPINE, cervical, paraplegia in injuries of (abs), 142
cervical, ruptured intervertebral disc in region of (abs), 143
etiology of osteochondritis of (abs), 868
extradural hemangioblastoma of, roentgenographically visualized with diodrast at operation and successfully removed (abs), 742
lumbar, roentgen anatomy of oblique view of, 699
lumbosacral, pseudarthrosis in (abs), 144

meningiomas and schwannomas of, diagnosis by myelography, 683
SPLENOMEGALY, congestive, hemorrhagic tendency in (abs), 433
SPONDYLITIS, ankylosing, early roentgen diagnosis of (abs), 141
rheumatoid (abs), 437
SPONDYLOLISTHESIS, etiology and frequency of, and its precursors (abs), 437
SPONGES, radiopaque, roentgen recognition of, 706
SPRUE, small intestinal pattern in, 658
STENOSIS, congenital hypertrophic, pyloric spasm simulating (abs), 124
congenital pulmonary (abs), 122
STEWART, THOMAS S., 1876–1949, obituary 853
STOMACH, adenocarcinoma of, and co-existent benign gastric ulcer, 677
carcinoma of (abs), 124
cytologic method as aid in diagnosis of carcinoma of (abs), 734
detection of carcinoma of, by photofluorographic methods, 183, 188
duodenal mechanism regulating motor and secretory activity of (abs), 277
mass roentgen survey of gastrointestinal tract to detect cancer of, 470
mucosal deformities of greater curvature of (abs), 429
procurement and critical appraisal of width diameter of midline retrogastric soft tissues, 56
prolapsed mucosa of, roentgen diagnosis, 784
simultaneous roentgenographic and gastroscopic examination of (abs), 277
vascular shunts in (E), 561
STREPTOMYCIN in miliary tuberculosis (abs,) 575
STRICTURE, acquired, of esophagus, surgical management of (abs), 427
SURGICAL research, use of isotopes in (abs), 288
SYNOVITIS, pigmented villonodular, of knee joint, roentgen diagnosis (abs), 435

TECHNIQUE, improvements in, in cerebral angiography (abs), 426
of bronchography in adults, 243
of direct cerebral angiography (abs), 266
of simple breast roentgenography (abs), 439
practical, for visualization of bronchial tree (abs), 272
rapid method of roentgen examination of small intestine, 45
TECHNIQUES for application of betatron to medical therapy, 591
of using radioisotopes as tracers, basic courses in, 570
TELECURIETHERAPY, results in mixed tumors of palate treated by, 82
TELEROENTGEN therapy, treatment of brucellosis by (abs), 873
TESTICLE, treatment of malignant tumors of (abs), 441
tumors of (abs), 285
TETRA-ETHYL AMMONIUM chloride, effect of, on gastric secretion and acidity in peptic ulcer (abs), 127
roentgen signs of altered alimentary function following autonomic blockade with (abs), 733
THIAMINE CHLORIDE, atypical adynamic ileus apparently caused by deficiency in (abs), 131
THIMBLE CHAMBER calibration on soft roentgen rays, 543
THIOCYANATE, effects of, on discharge of radioactive iodine from thyroid gland (abs), 881
THORAX See CHEST
THORIUM OXIDE, on use for radiation protection of gloves laden with (abs), 884
THYMONUCLEIC ACID synthesis, inhibition of, in tumor tissue by irradiation with roentgen rays (abs), 885
THYROID GLAND, accumulation of radioactive iodide by, in normal and thyrotoxic subjects (abs), 881
in children, uptake of radioactive iodine by normal and disordered (abs), 574
of rat, partial destruction of, by large doses of radioiodine, 731
preparation of radioautographs of tumors of, for study at high magnification (abs), 574
THYROIDITIS, subacute, and its treatment, 826
TISSUE reactions to fibrin film, effect of roentgen therapy on (abs), 263
TISSUES, post-pharyngeal lymphoid, roentgen treatment of infections of (abs), 438
retrogastric soft, procurement and critical appraisal of width diameter of midline, 56
TOMOGRAM, lateral thoracic, in normal subject (abs), 428
TONSILS, carcinoma of (abs), 582
roentgen treatment of infections of (abs), 438
TORULOSIS, roentgen findings in (abs), 269
TRACHEA, compression of, by anomalous innominate artery (abs), 573
TRACHEOESOPHAGEAL fistula and congenital atresia (abs), 123
TUBERCULIN test, quantitative, its significance in diagnosis of tuberculosis (abs), 575
TUBERCULOMAS, calcified intracranial (abs), 262
TUBERCULOSIS, acute miliary, possibilities of roentgen diagnosis of, 750
BCG vaccination in all age groups (abs), 428
chronic, possibilities of roentgen diagnosis of, 749
control, recent developments in (abs), 575
experience of United States Army in World War II (abs), 575
in Alabama State hospitals (abs), 575
medical and roentgenological aspects of mass chest surveys in, 147

miliary, Besnier-Boeck disease with transition into (abs), 580
miliary, streptomycin in (abs), 575
minimal, value of roentgenology in prognosis of, 153
program of Veterans Administration (abs), 574
protracted destructive, progressive Boeck's sarcoid associated with (abs), 580
pulmonary, carcinoma simulating (abs), 576
pulmonary, minimal, bronchial adenoma without signs of bronchial obstruction concomitant with, 209
pulmonary, reasons for common anatomic location of (abs), 119
pulmonary, simulating bronchogenic carcinoma (abs), 577
results and experiences from mass examinations for, in Copenhagen 1946 (abs), 428
significance of quantitative tuberculin test in diagnosis of (abs), 575
Tuberosity, lesser, of humerus, avulsion fracture of (abs), 139
Tuberculous dactylitis in adult (abs), 140
Tumor, adrenal, of liver in child (abs), 432
of posterior fossa, upward transtentorial herniation of brain stem and cerebellum due to (abs), 264
rare cranial, primary hemangioma of skull, 302
tissue, inhibition of ribo- and thymo-nucleic acid synthesis in, by irradiation with roentgen rays (abs), 885
Tumors, bone, experiences with (abs), 136
cartilaginous, of hand (abs), 139
experimental cerebral, irradiation of (abs), 585
giant cell, of bone (abs), 873
in mice, in vivo staining and retardation of, by acridine compounds (abs), 287
malignant, of rhinopharynx, roentgen diagnosis of (abs,) 427
malignant, of small intestine (abs), 738
malignant, of testis, treatment of (abs), 441
mixed, of palate, 82
of acoustic nerve (abs), 264
of testicle (abs), 285
thyroid, preparation of radioautographs of, for study at high magnification (abs), 574
Typhoid fever, acute intestinal obstruction in (abs), 125

Ulceration, benign, within duodenal diverticulum (abs), 430
Ulcers, primary nonspecific, of small intestine (abs), 431
Ulnocuneiform articulation, bilateral posttraumatic, 80
Ultraviolet radiation, effects of, on cornea (abs), 875
United States Army, tuberculosis experience of, in World War II (abs), 575
Ureter, primary benign neoplasm of (abs), 133
primary papillary carcinoma of (abs), 132
Urethane, effect of, on malignant diseases (abs), 286
Uterus, sarcoma of, 830; (abs), 876

Vagotomy in treatment of peptic ulcer (abs), 126; (abs), 127
Vascular disease, peripheral, in lungs, 17
disease, peripheral, study of, with radioactive isotopes (abs), 289
ligation, gastric ulcers produced experimentally by (abs), 127
Ventricles, cerebral, spontaneous rupture of (abs), 264
Vertebral angiography, 166
Veterans Administration, tuberculosis program of (abs), 574
Vomiting in infants, cardio-esophageal relaxation as cause of (abs), 266

Welders' siderosis, clearing of roentgen shadows in (abs), 119
Witwer, Eldwin R., 1890–1948, obituary, 108
portrait, 108

AUTHOR INDEX TO VOLUME 61

Adair, Frank E., 286
Adair, Norman, 281
Adams, G. D., 591
Adams, John M., 578
Alderson, B. Roxby, 135
Allen, J. Garrott, 885
Almy, G. M., 591
Andreasen, A. T., 138, 139
Angevine, D. Murray, 436
Antopol, W., 131
Arens, Robert A., 435
Arneson, A. N., 740
Arrowood, Julia G., 130
Astwood, E. B., 881
Atlee, Z. J., 588
Aubert, J., 869
Austin, V. T., 591
Axelrod, Arnold, 286

Bach, Theodore Franklin, 421
Bachrach, William H., 734
Baclesse, F., 427
Badgley, Carl E., 146
Baggenstoss, A. E., 575
Bailey, Wilbur, 437
Baily, Orville T., 263
Barclay, A. E., 883
Barden, Robert P., 17
Barnes, Roland, 142
Barron, E. S. Guzman, 884
Bartlett, Grant R., 884
Batt, Richard C., 274
Bazy, L., 869
Beatty, R. P., 134
Bechtol, Charles O., 137
Beneventi, F. A., 129
Benson, Clifford D., 430
Bercow, Celia, 219
Berenberg, William, 266
Berg, Benjamin N., 127
Berk, Morton E., 140
Berman, Lawrence, 286
Bernhard, C. Melvin, 432
Best, Arther, 881
Birath, Gosta, 577
Bjørnstad, Roar Th., 580
Black, B. Marden, 431
Blackwood, William 142
Blair, L. G., 121
Block, Malcolm, 734
Bloom, William, 855
Bockus, H. L., 429
Bogart, Franklin B., 873
Boone, William H., 511
Bost, Frederic C., 145
Bosworth, David M., 144
Bowing, Harry H., 517, 874, 878
Burke, Eugene M., 285
Brackin, John T., 677
Braestrup, Carl B., 397
Brailsford, James F., 136
Breed, J. Ernest, 416
Brewer, Arthur A., 278
Bromer, Ralph S., 248
Broustet, P., 732
Brown, B. R., 873
Brown, Walter, N., Jr., 808
Brues, Austin M., 880
Bucy, Paul C., 267
Bunting, Henry, 268
Burnett, W. Emory, 427
Burrows, H. Jackson, 141
Buschke, Wilhelm, 875

Cameron, Gordon H., 397
Camp, John D., 741, 881
Campbell, Harold W., 153
Campbell, Meredith F., 133
Carabello, N. C., 699
Carter, Ray A., 270
Case, James T., 414, 861
Casewell, H. Taylor, 427
Cave, Edwin F., 868
Chalecke, William E., 586
Chamberlain, W., Edward, 152, 726
Chamorro, A., 588
Chapman, William P., 130
Chatton, P., 428
Chèvremont, M., 886
Christie, Arthur C., 147
Clagett, O. Theron, 427
Clark, George L., 881
Clark, Stanley B., 275
Clerf, Louis H., 120
Cleveland, Mather, 144
Cobb, Cully A., Jr., 263
Cochrane, Archibald L., 153
Cohen, J. N., 690
Coleman, Claude C., 263
Colvert, James R., 125
Constant, George A., 134
Cooley, A. G., 557
Cooper, David A., 17, 37
Cooper, F. W., 289
Cooper, George, Jr., 281
Corrigan, K. E., 625, 839
Craver, Lloyd F., 581
Cross, James E., 283
Culver, Gordon J., 430
Cutler, Max, 82

Dailey, Morris E., 277
Daland, Ernest M., 283
D'Albora, John B., 577, 671
Dancoff, S. M., 591
Darby, E. K., 550
Dashiell, Grayson F., 432
David, Vernon C., 739
Davidoff, Leo M., 263, 317
Davies, H., 137
Day, F. H., 543
Dec, Joseph, 586
del Regato, J. A., 285, 875
Dell, J. M., Jr., 222, 436
Denier, Andre, 873
Denny-Brown, D., 281
Dennis, E. W., 289
DeSanctis, Adolph G., 868
Desjardins, A. U., 260
Dewulf, L., 872
Dexter, Lewis, 273
Dillon, Raymond A., 847
Dobson, R. L., 873
Dock, William, 119
Dockerty, Malcolm B., 139, 431, 735
Doig, A. T., 119
Donaldson, S. W., 146
Dorsey, Philip, 762
Doub, Howard P., 738
Dougherty, E. C., 879
Dowdy, Andrew H., 584
Dragstedt, Lester R., 128
Dratz, Henry M., 267
Dripps, Robert D., 23
Dry, Thomas J., 26
Dulac, G., 427

Eberhard, Theodore P., 871
Ecker, Arthur, 264
Edelstein, J. M., 133
Edson, John N., 577
Edwards, Jesse E., 38
Eisenberg, Stuart J., 369
Elkin, Daniel C., 289
Ellinger, Friedrich, 387
Ellis, Frank, 288
Engeset, Arne, 426
Epstein, Bernard S., 202, 275, 775
Ernst, Edwin C., 875
Etter, Lewis E., 699
Ettinger, Alice, 658, 742
Euphrat, Edwin J., 278
Evans, Robley D., 589
Evans, Titus C., 574
Evans, William A., Jr., 852
Evert, John A., 431
Eyherabide, Rodolfo, 457

Fairbank, H. A. Thomas, 134
Falle, E. De C., 124
Farris, Edmund J., 884
Fejer, E., 135

Feldman, Maurice, 429
Feldman, William H., 575
Felson, Benjamin, 432, 784
Ferrer, José M., Jr., 127
Fetter, John S., 366
Feuchtwanger, J. L., 438
Figi, F. A., 260
Fineman, Solomon, 324
Finkel, Miriam P., 880
Fischmann, E. J., 733
Fishback, H. R., Jr., 431
Fleischner, Felix G., 39, 199
Fletcher, Gilbert H., 209
Forbes, Robert, 282
Foster, Sidney E., 61
Fredericq, J., 886
Freed, John H., 884
Freudenthal, W., 579
Fricke, Robert E., 517, 878
Friedenwald, Jonas S., 875

Galluccio, Anthony C., 281
Gambill, Earl E., 739
Gardner, Clarence E., 580
Garland, L. Henry, 268
Gass, Charles C., 715
Gass, Harvey, 317
Gault, Edwin S., 422
Gay, Douglas M., 530
George, Murray P., 586
Gershon-Cohen, J., 277, 557
Gianquinto, Peter J., 577
Gianturco, Cesare, 584
Gilchrist, R. K., 739
Gilfillan, Clarence D. N., 272
Gilmore, John H., 281
Glaser, Kurt, 482
Glasser, Samuel M., 387
Golden, Ross, 54
Goldfeder, Anna, 881
Goldman, Lester, 131
Good, C. Allen, 26
Graham, Ruth, 734
Green, Thomas H., 734
Greenberg, B. B., 140
Greenfield, Henry, 434
Greening, Roy, 874
Greening, Roy R., 269
Grobman, Arnold B., 98
Gross, Robert E., 123, 573
Gross, S. W., 426
Guralnick, Eugene, 283
Guy, Chester C., 123
Guzman, Leonardo, 876
Gwynne, F. J., 733

Hagey, Helen, 145
Halberstaedter, L., 586
Hale, Clayton H., 583
Hale, Nathan G., 132
Hamernik, J. F., 875
Hamilton, J. G., 587
Hamilton, J. J. S., 550
Hammer, J. M., 839
Hanelin Joseph, 735
Hankins, Walter D., 280
Hansen, Paul Scott, 125
Hanson, A. O., 591
Hardesty, Kile C., 711
Hardisty, N. M., 260
Hare, Hugh F., 829
Harrington, Stuart W., 126
Harrison, C. V., 137
Hatchett, Capres S., 715
Hauser, Emil D. W., 134
Hawley, Chapin, 784
Hawley, Paul R., 574
Haxthausen H., 579
Hayden, H. S., 839
Hecht, P. L., 742
Heckel, George P., 741
Heifetz, Carl J., 128
Heilbrun, Norman, 434
Henshaw, P. S., 879
Herbut, Peter A., 120
Herrmann, Julian B., 286
Heublein, Gilbert W., 272
Higgason, John M., 402
Hilleboe, Herman E., 575
Hinkel, C. L., 335
Hinshaw, H. Corwin, 575
Hitchock, Harold H., 137
Hodges, Fred J., 265, 733, 735
Holden, Lawrence B., 166
Hollingsworth, R. K., 271
Holm, Mogens, 428
Holm, Sigrid, 428
Holmes, Barbara E., 885
Holmes, George W., 583
Holt, John F., 274, 733
Horwitz, Thomas, 144
Howarth, Frank, 288
Hubay, Charles A., 493
Hughes, E. S. R., 867
Hughes, Felix A., Jr., 122
Huguier, J., 869
Humphreys, George H., II, 461
Hunsberger, W. G., 146

Ickowicz, M., 586
Imler, Allison E., 873
Immermann, E. William, 137
Ingegno, Alfred P., 577, 671
Ingraham, Franc D., 263

Jacobson, L. O., 590, 885
Jacobsson, Folke, 872
Jamison, Horace W., 270
Jenkins, Hilger P., 128
Jenkinson, E. L., 875
Jennings, W. A., 863
Johns, H. E., 550
Jones, Glenn E., 586
Jonsson, Gunnar, 867
Joplin, R. J., 434

Kane, F. F., 125
Kaplan, Gustave, 626
Kaplan, Henry S., 268
Kelby, G. M., 441, 576
Kemp, F. H., 868
Kennedy, Thomas J., 517
Kerley, T. G., 591
Kerst, D. W., 591
Kinzer, Richard E., 212
Kirschon, Alice, 885
Kittle, C. Frederick, 128
Klein, A., 434
Knauss, Harold P., 880
Koch, H. W., 591
Koenig, E. C., 275, 430
Koven, A. Link, 578
Kratzman, Emil A., 511
Kristoff, Frederic V., 143, 267
Krosnick, Gerald, 291
Kuhn, William G., 434
Kvadsheim, Hans, 426

Lam, Conrad R., 272
Lame, Edwin L., 428, 439, 443
Lanari, Alfredo, 733
Landauer, Robert S., 588
Lange, Kurt, 589
Lanzl, E. F., 591
Lanzl, L. H., 591
Larsen, Loren J., 145
Lasnitzki, Illse, 287
Laubry, P., 869
Laughlin, J. S., 591
Lawrence, J. H., 873, 879
Leighton, Robert S., 245
Leitch, James L., 530
Leithauser, D. J., 131
Lemone, David V., 578
LeRoy, George V., 455
Leslie, E. I., 428
Leucutia, T., 104, 408, 636
Levi, Leo M., 380
Lewis, Margaret Reed, 287
Lewis, Raymond W., 435
Lindgren, E., 266
Lindsay, Stuart, 870
Lingley, James R., 438
Lipp, Charles S., 584
Lisco, Hermann, 880
List, Carl F., 265
Loebell, M. A., 580
Loewinsohn, E., 428
Long, Esmond R., 575
Longmire, William P., Jr., 123

Loverdo, André, 884
Low-Beer, B. V. A., 873
Lyons, Richard H., 733

MacCarty, William C., 584
McClement, Patricia, 397
McClure, G. Y., 591
McCune, Donovan J., 574
McDonnell, D. P., 138
McGavran, H. G., 133
McGuff, Paul, 735
Macht, David I., 534
Macht, Stanley H., 100
McIndoe, A. H., 282
Mack, Pauline Berry, 808
McLaughlin, A. I. G., 119
Magee, R. K., 432
Mahan, Thomas K., 281
Maleki, A., 428
Mahoney, Earle B., 586
Mallet, Lucien, 589
Manjunath Rai, K., 872
Marcus, S. M., 133
Marks, E. K., 590
Martin, J. H., 286
Mason, Joyce, 734
Maurin, Robert, 589
Means, J. H., 864
Mednick, E., 56
Melick, W. F., 132
Menville, Leon J., 269
Merner, T. B., 440
Metz, Arthur R., 128
Meyer, Karl A., 126, 127
Meyer, Paul D., 784
Milch, Henry, 80
Milham, Mary, 885
Miller, Clark F., 506
Miller, Edwin, 130
Miller, Joseph M., 677
Miller, Leon L., 586
Miller, W. B., 289
Miller, Zelma B., 884
Mills, William L., 366
Mitchell, J. S., 287
Mixer, Harry W., 279
Moe, Gordon K., 733
Moehlig, Robert C., 797
Moir, William W., 436
Moore, Francis D., 288
Moore, Sherwood, 470, 578
Moretz, William H., 280
Morgan, Russell H., 183, 188
Morton, James A., 583
Moses, Sylvia G., 875
Mueller, J., 580
Mueller, Wilbur K., 402
Murphy, Douglas P., 884
Murphy, J. P., 77
Murphy, William P., Jr., 847

Myers, Leonard A., 279

Naiman, Dorothy Neuhof, 95
Narins, Lester, 91
Neary, G. J., 877
Neligh, Rosalie B., 733
Neuhauser, Edward B. D., 263, 266, 573
Neville, George A., 530
Newell, R. R., 718, 726
Nolan, James F., 876
Norris, Chas. M., 120

Odom, Guy L., 143
Oleck, Henry T., 123
O'Loughlin, Bernard J., 275
Olsen, Arthur M., 573
Olsson, Olle, 426
Oscherwitz, Daniel, 263
Osgood, Ellis C., 736
Osmond, John D., Jr., 826
Ostro, Marcus, 534
Ostrum, Herman W., 443
Ould, Carlton L., 277

Pack, George T., 870
Palazzo, William L., 439
Palmer, Walter L., 432
Parsons, P. B., 680
Paterson, Ralston, 863
Patterson, William M., 281
Paul, Lester W., 436
Pautrier, L. M., 578
Pearse, Herman E., 586
Pearson, I. A., 839
Peck, Willis S., 236
Pedrazzini, A., 580
Pein, N. K., 124
Pelner, Louis, 690
Penberthy, Grover C., 430
Pendergrass, Eugene P., 428, 439, 443, 884
Perry, T., 876
Peyton, William T., 143
Pfahler, George E., 853
Pirkey, E. L., 875
Pohle, Ernst A., 284, 583
Polgar, Francis, 637
Pollard, H. Marvin, 734
Polley, Howard F., 437
Poppel, M. H., 56, 219
Portmann, U. V., 826
Potts, Willis J., 130
Powell, Chester B., 166
Prosser, C. Ladd, 882
Pugh, David G., 739
Pusch, Lewis C., 720

Quastler, H., 591
Quimby, Edith H., 574

Ramsey, George H., 586
Randall, Lawrence M., 735
Randall, W. Spears, 354, 365
Raper, John R., 585
Reboul, H., 869
Refvem, Olav, 579
Reich, Leo, 260
Reich, Stanley B., 830
Reidy, J. A., 434
Reilly, William A., 870
Richardson, W., 284
Richter, Maurice N., 868
Riesen, D. E., 591
Rigler, Leo G., 279, 576, 743
Riley, E. F., 879
Ritchey, Hardin, 267
Ritvo, M., 124, 291
Roach, John F., 183, 188
Robbins, L. L., 284, 438
Robertson, Harold D., 586
Robinson, C. S., Jr., 591
Rogers, James V., Jr., 706
Rogers, T. H., 589
Rolleston, G. L., 141
Romano, Nicolás, 457
Rorher, R. H., 289
Rosenberg, F. Edward, 435
Rosenthal, Sol R., 428
Rosi, Peter A., 126
Rossitto, Anthony F., 438
Roswit, Bernard, 387, 626
Rothstein, Emil, 195
Rottenberg, Louis A., 461
Rundles, R. Wayne, 735
Russ, S., 863
Russakoff, A. H., 575
Russo, Peter E., 281

Saenger, Eugene L., 436
Sahyoun, Philip F., 369
Sampson, D. Alan, 431
Sanderson, Margaret, 885
Sante, L. R., 1, 40
Sarnoff, Stanley J., 130
Sauer, Hans R., 285
Scarpellino, Louis A., 279
Schilling, John A., 586
Schlesinger, P. T., 150
Schmidt, Herbert W., 427
Scholl, A. J., 433
Schottstaedt, Edwin R., 145
Schulz, Milford D., 582
Scott, Wendell G., 37, 578
Scoville, William B., 280
Seldin, Donald W., 268
Seltz, Herman, 432
Senturia, H. R., 128
Shackman, Ralph, 137
Shauffer, I. A., 124, 291
Shea, Patrick, 289

Sheinmel, A., 56
Shelliton, John G., 139
Siebert, Walter J., 741
Sievert, Rolf M., 289
Siltzbach, Louis E., 576
Simmons, Donald R., 143
Simon, Norman, 91
Singleton, A. C., 411
Skaggs, L. S., 232, 591
Sloan, Robert D., 183, 188
Slocumb, Charles H., 437
Smith, Lawrence W., 422
Smith, Rector, 584
Solovay, H. U., 475
Solovay, Julius, 475
Sosman, Merrill C., 273, 364
Soubrié, Alberto, 733
Speert, Harold, 877
Spencer, Jack, 736
Spillman, Ramsay, 102, 722
Stambro, William, 876
Stanley, Malcolm M., 881
Stapleton, G. E., 879
Stapleton, J. G., 435
Stauffer, Herbert M., 431
Stein, I, F., 126, 127
Stein, Samuel C., 153
Steinberg, Israel, 41
Steinhausen, Theodore B., 586
Stenstrom, K. W., 440, 441
Stephens, H. Brodie, 122
Stokes, Robert F., 855
Stout, Arthur Purdy, 461
Strain, William H., 586
Stroud, Leona, 881
Sugar, Oscar, 166
Swenson, Paul C., 341

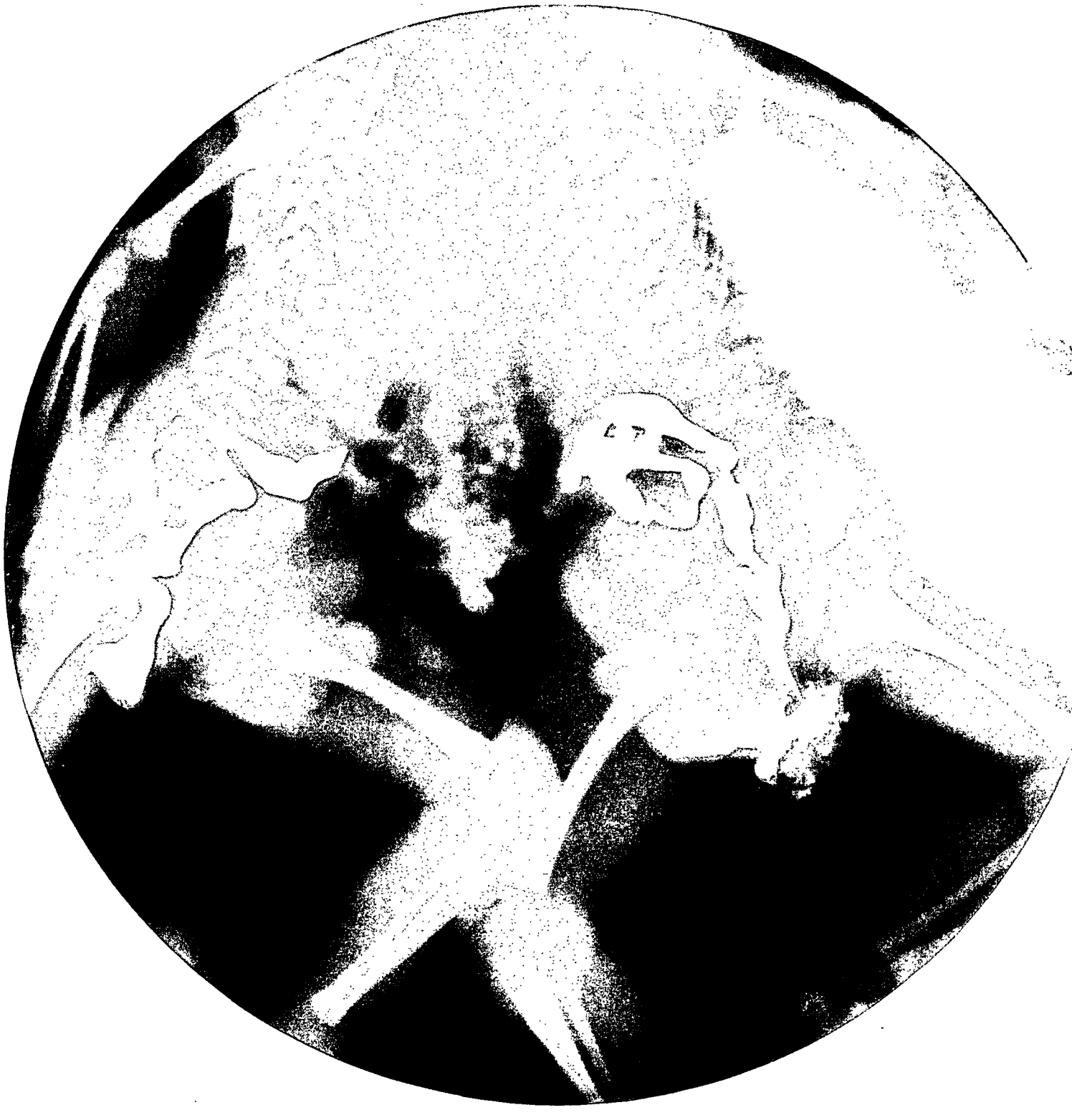
Tansley, Katharine, 585
Tarlov, I. M., 742
Taylor, Alexander R., 142
Taylor, H., 124
Taylor, Lauriston S., 726
Teplick, J. George, 762
Thaxter, Langdon T., 736
Thomas, Sydney F., 432
Thompson, E. A., 591
Thompson, Frederick R., 144
Tocantins, Leandro M., 433
Tomlinson, Carol, 284
Torkildsen, Arne, 264
Trapp, Hughes Daniel, 808
Troland, Charles E., 263
Trout, E. D., 588
Trump, J. G., 234
Twinem, F. P., 129

Uhlmann, Erich M., 232
Ulfelder, Howard, 734
Umansky, A. L., 140
Ungerleider, Harry E., 275

Vaccarezza, Raul F., 733
Valle, Anibal Roberto, 577
Varga, Charles, 868
Vaughan, C. E., 435
Vaughan, L. M., 260
Vincent, Helen Whitgrove, 584
Vincent, James G., 584
Vitt, A. E., 132

Walk, L., 243
Walker, H. John, 582
Wasson, W. Walter, 30, 874
Waterman, George W., 875
Watkins, W. Warner, 869
Watson, Ernest M., 285
Waugh, John M., 735
Wearing, J. D. H., 120
Wechsler, S., 426
Weens, H. S., 262, 706
Weig, Clayton G., 430
Weintraub, Sydney, 45
Welch, C. S., 742
Westphal, Kean F., 122
Wheeler, Digby, 738
White, M. Lawrence, Jr., 577
Williams, Robert G., 41, 45
Wilner, Daniel, 341
Wilson, C. W., 585
Wilson, D. C., 868
Wilson, John C., 138
Windeyer, B. S., 282
Windholz, Frank, 61, 439, 442, 582
Winge, Knud, 428
Wolff, Brigitte, 288
Wood, Ernest H., Jr., 683
Woodard, Helen Q., 286
Woodruff, G. Eugene, 575
Wyatt, George M., 354
Wyckoff, Harold, 726
Wyke, B. D., 302

Zanca, Peter, 278
Zimmer, Johannes, 738

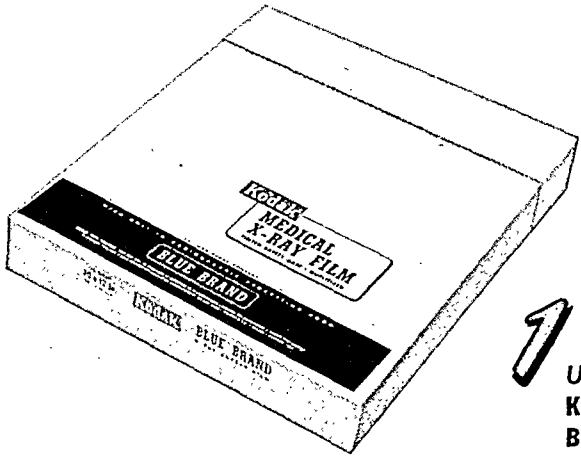


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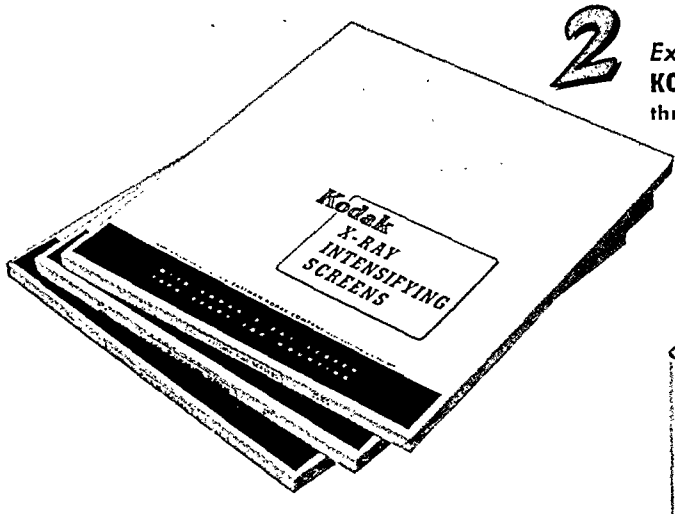
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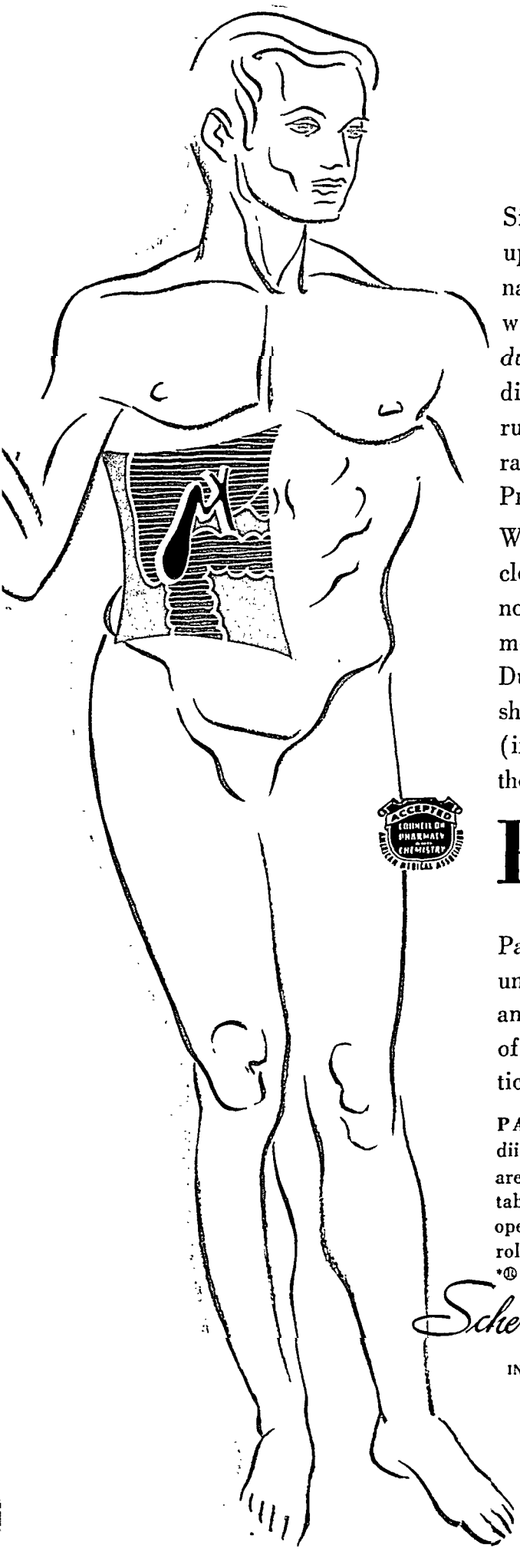
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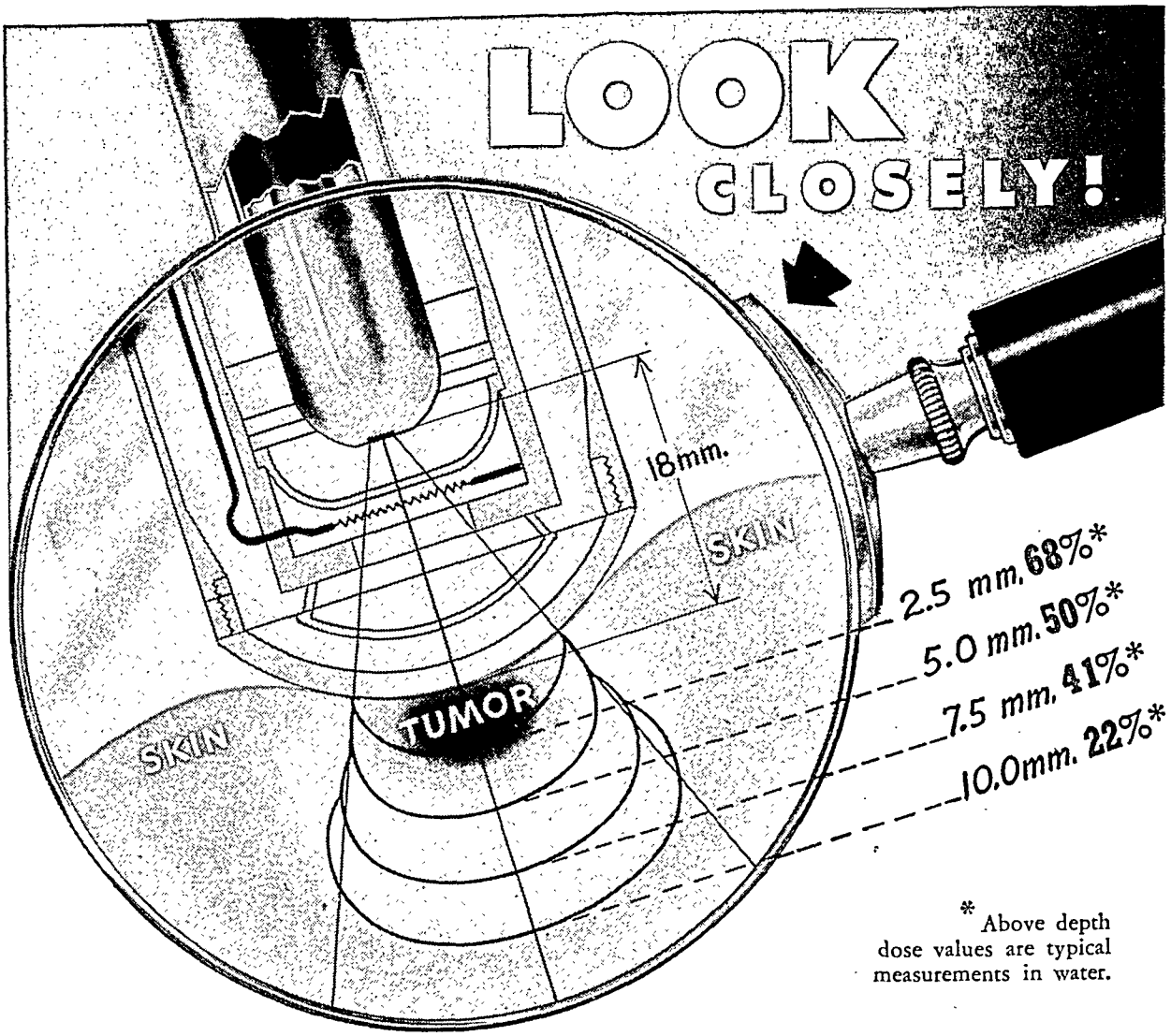


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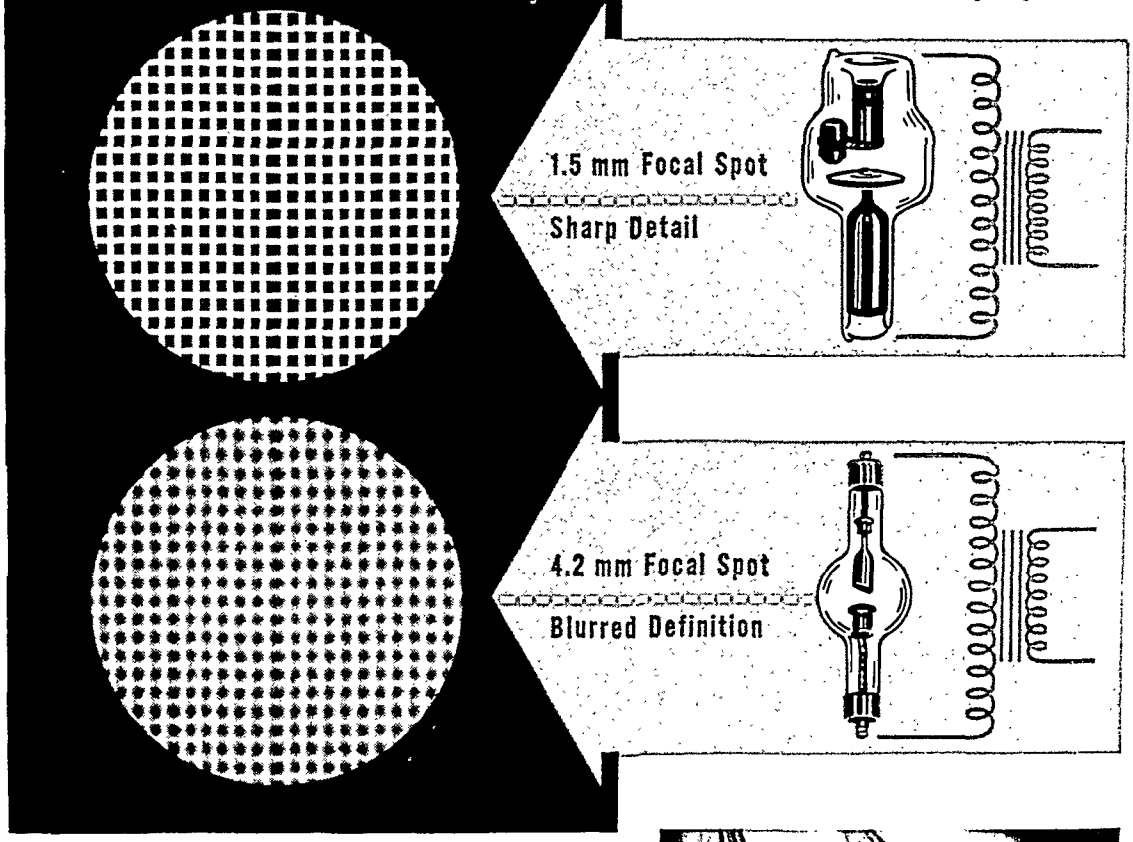
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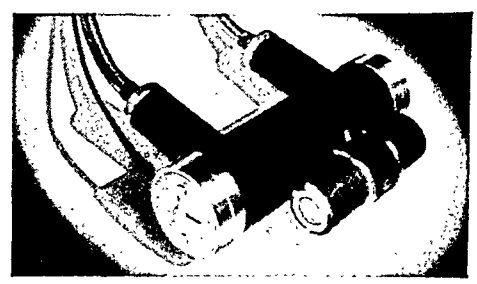
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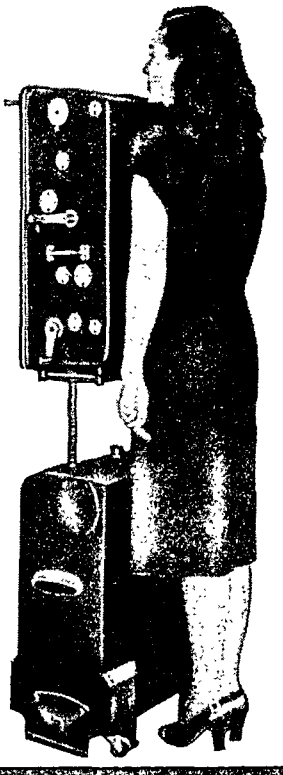
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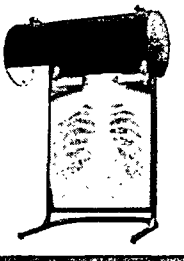
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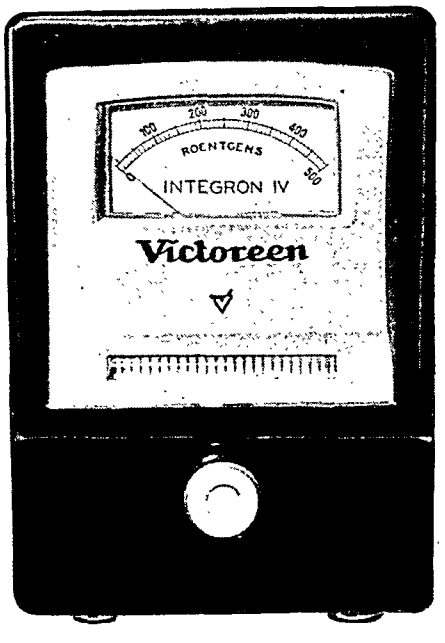
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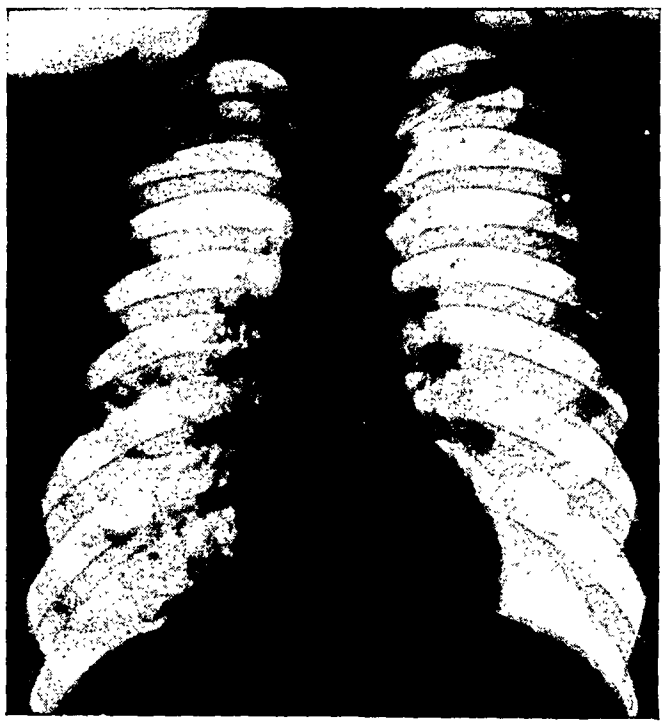
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CONTENTS OF VOLUME 61

ORIGINAL ARTICLES

The Anatomy and Physiology of the Lesser Circulation as Indicated by its Behavior in Health and Disease	*L. R. Sante, M.D.*	1
Peripheral Vascular Disease in the Lungs	*Robert P. Barden, M.D.* *David A. Cooper, M.D.*	17
Lung Function	*Robert D. Dripps, M.D.*	23
Conditions Which Result in Increased Pressure within the Lesser Circulation	*E. Allen Good, M.D.* *Thomas J. Dry, M.D.*	26
The Evaluation of the Lesser Circulation as Portrayed by the Roentgenogram	*W. Walter Wasson, M.D.*	30
The Value of Angiocardiography in Establishing the Diagnosis of Pericarditis with Effusion	*Robert G. Williams, M.D.* *Israel Steinberg, M.D.*	41 41
A Rapid Method of Roentgenologic Examination of the Small Intestine. A Preliminary Report	*Sydney Weintraub, M.D.* *Robert G. Williams, M.D.*	45
The Procurement and Critical Appraisal of the Width Diameter of the Midline Retrogastric Soft Tissues	*M. H. Poppel, M.D., F.A.C.R.* *A. Sheinmel, M.D.* *E. Mednick, M.D.*	56
Bone Sclerosis in Leukemia and in Non-leukemia Myelosis	*Frank Windholz, M.D.* *Sidney E. Foster, M.D.*	61
Lumbar Intervertebral Disc Protrusion Contralateral to the Side of Symptoms and Signs; Myelographic Verification in Two Cases	*J. P. Murphy, M.D.*	77
Bilateral Posttraumatic Ulnocuneiform Articulation	*Henry Milch, M.D.*	80
Mixed Tumors of the Palate	*Max Cutler, M.D.*	82
The Effect of Hyaluronidase on the Absorption of a Subcutaneously Deposited Radiopaque Substance	*Norman Simon, M.D.* *Lester Narins, M.D.*	91
Effect of Roentgen Rays upon Bartonella-Infected and Normal Rats	*Dorothy Neuhof Naiman, Ph.D.*	95
On the Association of Certain Hematomas with Myelencephalic Blebs in the House Mouse	*Arnold B. Grobman, Ph.D.*	98
A New Processing Room Accessory: The "Clip Drip" Tray	*Stanley H. Macht, M.D.*	100
Trifocal Glasses as an Aid to the Older Roentgenologist	*Ramsay Spillman, M.D.*	102
Some Medical and Roentgenological Aspects of Mass Chest Surveys	*Arthur C. Christie, M.D.*	147
The Value of Roentgenology in the Prognosis of Minimal Tuberculosis	*Archibald L. Cochrane* *Harold W. Campbell* *Samuel C. Stein*	153
Vertebral Angiography	*Oscar Sugar* *Lawrence B. Holden* *Chester B. Powell*	166
The Detection of Gastric Carcinoma by Photofluorographic Methods. Part I. Introduction	*John F. Roach* *Robert D. Sloan* *Russell H. Morgan*	183
The Detection of Gastric Carcinoma by Photofluorographic Methods. Part II. Equipment Design	*John F. Roach* *Robert D. Sloan* *Russell H. Morgan*	188
The Azygos Lobe: Its Involvement in Pulmonary Disease	*Emil Rothstein, M.D.*	195
Occurrence and Diagnosis of Dilatation of		

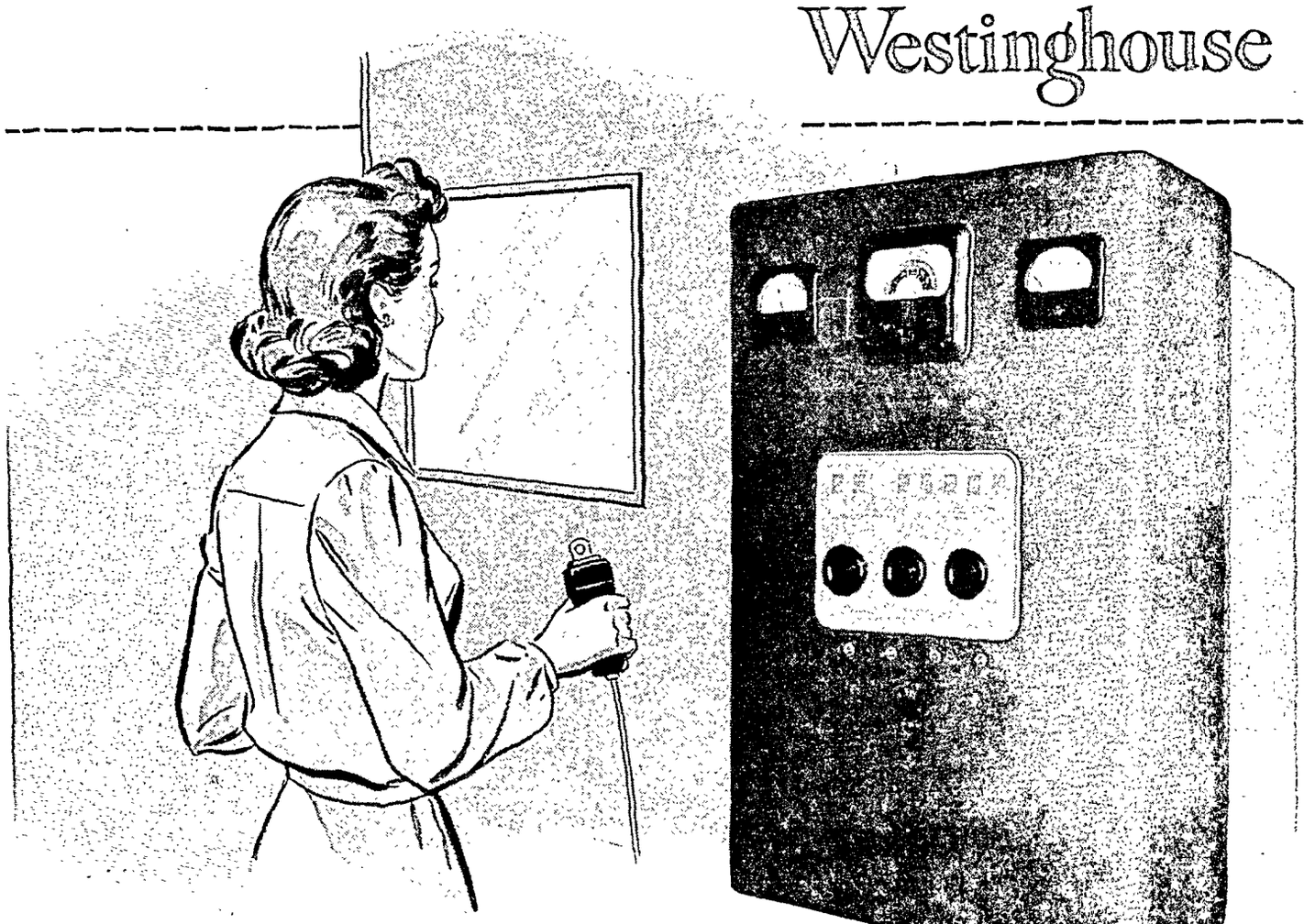
the Aorta Distal to the Area of Coarctation	*Felix G. Fleischner*	199
Left Atrial Calcification in Rheumatic Heart Disease	*Bernard S. Epstein, M.D.*	202
A Case of Bronchial Adenoma without Signs of Bronchial Obstruction, Concomitant with Minimal Pulmonary Tuberculosis	*Captain Gilbert H. Fletcher, M.C.* *Marion S. Lombard.*	209
Intraluminal Diverticulum and Other Lesions Producing Intermittent Duodenal Obstruction or Stasis	*Richard E. Kinzer, M.D.*	212
The Roentgen Manifestations of Pancreatitis Complicating Mumps	*M. H. Poppel, M.D., F.A.C.R.* *Celia Bercow, M.D.*	219
Demonstration of Sinus Tracts, Fistulas and Infected Cavities by Lipiodol	*Major James M. Dell, Jr., M.C.*	223
Principles of Fast Electron Therapy in Cancer	*Erich M. Uhlmann, M.D., F.A.C.R.* *Lester S. Skaggs, Ph.D.*	232
Part Time Radiological Practice in Hospitals of Small Cities	*Willis S. Peck, M.D.*	236
Contribution to the Technique of Bronchography in Adults	*L. Walk*	243
Malleable Cones for Roentgen Therapy	*Robert S. Leighton, M.D.*	245
The Clinical and Roentgen Manifestations of Erythroblastosis Fetalis	*Max Ritvo, M.D.* *Irving A. Shauffer, M.D.* *Gerald Krosnick, M.D.*	291
Primary Hemangioma of the Skull: A Rare Cranial Tumor	*B. D. Wyke, M.B., B.S.*	302
Convolutional Markings in the Skull Roentgenograms of Patients with Headache	*Leo M. Davidoff, M.D.* *Harvey Gass, M.D.*	317
A Practical Serialograph for Intracranial Angiography	*Solomon Fineman, M.D., M.A.*	324
Unresolved Pneumonia: An Exclusion Diagnosis	*C. L. Hinkel, M.D., Med. Sc.D.*	335
Unfused Ossification Centers Associated with Pain in the Adult	*Paul C. Swenson, M.D.* *Daniel Wilner, M.D.*	341
Monostotic Fibrous Dysplasia	*George M. Wyatt, M.D.* *W. Spears Randall, M.D.*	354
Regional Ileitis (Cicatrizing Enteritis) of Prenatal Origin	*John S. Fetter, M.D.* *William L. Mills, M.D.*	366
Hodgkin's Disease: A Histopathological and Clinical Classification with Radiotherapeutic Response	*Philip F. Sahyoun, M.D.* *Stuart J. Eisenberg, M.D.*	369
The Roentgen Treatment of Cutaneous Carcinoma Involving Cartilage	*Leo M. Levi, M.D.*	380
The Treatment of Radiation Sickness and Adrenal Cortical Hormone (Desoxycorticosterone Acetate)	*Friedrich Ellinger, M.D.* *Bernard Roswit, M.D.* *Samuel M. Glasser, M.D.*	387
Depth Dose Measurements for 250 kv. Roentgen Rays.	*Carl B. Braestrup* *Gordon H. Cameron* *Patricia McClement.*	397
Spot Scanography: Method of Determining Bone Measurement	*Wilbur K. Mueller, M.D.* *John M. Higgason, M.D.*	402
Hemosiderosis of the Lung Due to Mitral Disease	*Eugene P. Pendergrass, M.D.* *Edwin L. Lame, M.D.* *Herman W. Ostrum, M.D.*	443
The Apical Form of Bronchopulmonary Cancer	*Dr. Nicolas Romano* *Dr. Rodolfo Eyherabide*	457
A Case of Carcinosarcoma of the Esophagus	*Arthur Purdy Stout, M.D.* *George H. Humphreys, II, M.D.* *Louis A. Rottenberg, M.D.*	461

Mass Roentgenological Survey of the Gastrointestinal Tract to Detect Cancer of the Stomach	*Sherwood Moore, M.D.*	470
Paraplegic Neuroarthropathy	*Julius Solovay, M.D.* *H. U. Solovay, M.D.*	475
Double Contour, Cupping and Spurring in Roentgenograms of Long Bones in Infants	*Kurt Glaser, M.D.*	482
Sesamoid Bones of the Hands and Feet	*Charles A. Hubay, M.D.*	493
Occupational Calcareous Peritendinitis of the Feet	*Clark F. Miller, M.D.*	506
Kaposi's Sarcoma	*William H. Boone, M.D.* *Emil A. Kratzman, M.D.*	511
Radium Therapy for Carcinoma of Bartholin's Glands	*Harry H. Bowing, M.D.* *Robert E. Fricke, M.D.* *Thomas J. Kennedy, M.D.*	517
Effects of Repeated Low Doses of Neutrons on the Estrous Cycle of the White Rat	*James L. Leitch, Ph.D.* *Douglas M. Gay, M.D.* *George A. Neville*	530
Pharmacological Reactions of Sera and Drugs Irradiated with Roentgen Rays of Varying Wavelength	*David I. Macht* *Marcus Ostro*	534
Thimble Chamber Calibration on Soft Roentgen Rays.	*F. H. Day.*	543
A Negative Feedback Dosage Rate Meter Using a Very Small Ionization Chamber	*H. E. Johns* *E. K. Darby* *J. J. S. Hamilton*	550
Roentgenographic Facsimile: A Rapid Accurate Method for Reproducing Roentgenograms at a Distance via Wire or Radio Transmission.	*J. Gershon-Cohen, M.D.* *A. G. Cooley*	557
Techniques for Application of the Betatron to Medical Therapy	*H. Quastler* *G. D. Adams* *G. M. Almy* *S. M. Dancoff* *A. O. Hanson, D. W. Kerst,* *H. W. Koch* *L. H. Lanzl* *J. S. Laughlin* *D. E. Riesen* *C. S. Robinson, Jr.* *V. T. Austin* *T. G. Kerley* *E. F. Lanzl* *G. Y. McClure* *E. A. Thompson* *L. S. Skaggs*	591
The Role of Nitrogen Mustard (HN_2) as a Systemic Adjunct to the Radiation Therapy of Certain Malignant Diseases	*Bernard Roswit, M.D.* *Gustave Kaplan, M.D.*	626
Studies on Respiratory Mechanics	*Francis Polgar, M.D.*	637
Small Intestinal Pattern in Sprue and Similar Deficiency Diseases	*Alice Ettinger, M.D.*	658
Double Gallbladder	*Alfred P. Ingegno, M.D.* *John B. D'Albora, M.D.*	671
Co-existent Benign Gastric Ulcer and Adenocarcinoma of the Stomach	*John T. Brackin, M.D.* *Joseph M. Miller, M.D.*	677
Adenocarcinoma of the Jejunum	*P. B. Parsons, M.D.*	680
The Diagnosis of Spinal Meningiomas and		

Schwannomas by Myelography	*Ernest H. Wood, Jr., M.D.*	683
Osteogenesis Imperfecta Tarda	*Louis Pelner, M.D.* *J. N. Cohen, M.D.*	690
Roentgen Anatomy of Oblique Views of the Lumbar Spine	*Lewis E. Etter, M.D.* *N. C. Carabello, M.D.*	699
Roentgenologic Recognition of Radiopaque Sponges	*H. Stephens Weens, M.D.* *James V. Rogers, Jr., M.D.*	706
Sterile Pyuria	*Kile C. Hardesty, M.D.*	711
A Simple, Inexpensive Set of Prisms for Viewing Stereoscopic Roentgenograms	*Charles C. Gass, M.D.* *Capres S. Hatchett, M.D.*	715
The Possibilities and Limitations of Roentgen Diagnosis	*Leo G. Rigler, M.D.*	743
The Roentgen Findings in Intracranial Mass Lesions	*J. George Teplick, M.D.* *Philip Dorsey, M.D.*	762
Complete Block of the Lumbar Spinal Canal Due to Herniation of the Nucleus Pulposus	*Bernard S. Epstein*	775
The Roentgenologic Diagnosis of Prolapsed Gastric Mucosa	*Chapin Hawley, M.D.* *Paul D. Meyer, M.D.* *Benjamin Felson, M.D.*	784
Arachnodactyly (Marfan's Syndrome)	*Robert C. Moehlig, M.D.*	797
The Quantitative Evaluation of Bone Density	*Pauline Beery Mack* *Walter N. Brown, Jr.* *Hughes Daniel Trapp*	808
Subacute (Pseudotuberculous, Giant Cell) Thyroiditis and Its Treatment	*John D. Osmond, Jr., M.D.* *U. V. Portmann, M.D.*	826
Sarcoma of the Uterus	*Stanley B. Reich, M.D.*	830
Studies on the Metabolism of Radioisotopes by Various Fungi and Bacteria	*I. A. Pearson* *J. M. Hammer* *K. E. Corrigan* *H. S. Hayden*	839
Portable Projector for Roentgenograms	*Raymond A. Dillon, M.D.* *William P. Murphy, Jr., M.D.*	847

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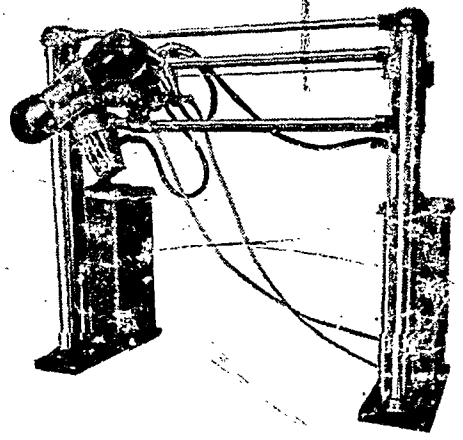
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